* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	SEP 09	ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS 4	OCT 03	MATHDI removed from STN
NEWS 5	OCT 04	CA/CAplus-Canadian Intellectual Property Office (CIPO) added to core patent offices
NEWS 6	OCT 13	New CAS Information Use Policies Effective October 17, 2005
NEWS 7	OCT 17	STN(R) AnaVist(TM), Version 1.01, allows the export/download of CAplus documents for use in third-party analysis and visualization tools
NEWS 8	OCT 27	Free KWIC format extended in full-text databases
NEWS 9	OCT 27	DIOGENES content streamlined
NEWS 10	OCT 27	EPFULL enhanced with additional content
NEWS 11	NOV 14	CA/CAplus - Expanded coverage of German academic research

NEWS EXPRESS NOVEMBER 18 CURRENT VERSION FOR WINDOWS IS V8.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005. V8.0 USERS CAN OBTAIN THE UPGRADE TO V8.01 AT http://download.cas.org/express/v8.0-Discover/

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FILE 'HOME' ENTERED AT 18:51:56 ON 22 NOV 2005

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 18:52:03 ON 22 NOV 2005
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 NOV 2005 HIGHEST RN 868586-21-4
DICTIONARY FILE UPDATES: 21 NOV 2005 HIGHEST RN 868586-21-4

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

```
**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************
```

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

```
=> file hcaplus
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   0.43       0.64

FILE 'HCAPLUS' ENTERED AT 18:52:06 ON 22 NOV 2005
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FILE COVERS 1907 - 22 Nov 2005 VOL 143 ISS 22
FILE LAST UPDATED: 21 Nov 2005 (20051121/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s affective () disorder?
          3976 AFFECTIVE
             3 AFFECTIVES
          3978 AFFECTIVE
                 (AFFECTIVE OR AFFECTIVES)
        409471 DISORDER?
L1        2114 AFFECTIVE (W) DISORDER?
```

```
=> s l1 and review/dt
      1873001 REVIEW/DT
L2          599 L1 AND REVIEW/DT

=> s l2 and autism
         1297 AUTISM
L3          8 L2 AND AUTISM

=> d l3, ibib abs, 1-8
```

L3 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Chng References

ACCESSION NUMBER: 2005:970365 HCAPLUS
TITLE: Immunological etiology of major psychiatric disorders: evidence and therapeutic implications
AUTHOR(S): Sperner-Unterweger, Barbara
CORPORATE SOURCE: Department of Biological Psychiatry, Innsbruck University Clinics, Innsbruck, Austria
SOURCE: Drugs (2005), 65(11), 1493-1520
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Historically, immunol. research in psychiatry was based on empirical findings and early epidemiol. studies indicating a possible relation between psychiatric symptoms and acute infectious diseases. However, aetiopathol. explanations for psychiatric disorders are no longer closely related to acute infection. Nevertheless, immune hypotheses have been discussed in schizophrenia, **affective disorders** and infantile **autism** in the last decades. Although the variability between the results of the epidemiol. studies conducted to date is strikingly high, there is still some evidence that the immune system might play a role in the aetiopathogenesis of these three psychiatric diseases, at least in subgroups of patients. In anxiety disorders immunol. research is still very much in its infancy, and the few and inconsistent data of immune changes in these patients are believed to reflect the influence of short- or long-term stress exposure. Nevertheless, there are also some hints raising the possibility that autoimmune mechanisms could interrupt neurotransmission, which would be of significance in certain patients with anxiety, and panic disorders. Drug and alc. (ethanol) dependence are not believed to be primarily influenced by an immunol. etiol. Immune reactions due to different drugs of abuse and alc. may directly or indirectly influence the course of concomitant somatic diseases. In different org. brain disorders the underlying somatic disease is defined as a primary immune or autoimmune disorders, for example AIDS and SLE. Therapeutic approaches in Alzheimer's disease also apply immunol. methods such as strategies of active/passive immunization and NSAIDs. Considering the comprehensive interactive network between mind and body, future research should focus on approaches linking targets of the different involved systems.

REFERENCE COUNT: 408 THERE ARE 408 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Chng References

ACCESSION NUMBER: 2004:31945 HCAPLUS

DOCUMENT NUMBER: 140:197018
TITLE: Genetic analysis of psychiatric disorders associated with human chromosome 18
AUTHOR(S): Kamnasaran, Deepak
CORPORATE SOURCE: The Arthur and Sonia Labatts Brain Tumour Research Centre, The Hospital for Sick Children, Toronto, ON, Can.
SOURCE: Clinical and Investigative Medicine (2003), 26(6), 285-302
CODEN: CNVMDL; ISSN: 0147-958X
PUBLISHER: Canadian Medical Association
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Current models on the etiol. of psychiatric disorders support the idea of a biol. cause as well as interactions of biol. systems with the environment. The elucidation of the genetic etiol. is of paramount importance to understand the cause of psychiatric disorders. Human chromosome 18 was identified as one of the first chromosomes to be aberrant in psychiatric patients and has subsequently served as a model to identify the mol. cause. In this article I review a multitude of methodologies that can be used in detg. the genetic basis of schizophrenia, **affective disorder** and **autism** assocd. with human chromosome 18. These strategies include the use of chromosome aberrations, linkage and assocn. studies, mouse-human comparative genomics, mutation anal. on candidate genes, trinucleotide repeat expansion studies, search for genes demonstrating parental effects and bioinformatics. Current data from the use of these methods are cited from the literature. Linkage and assocn. studies have suggested at least 2 candidate loci on the short and long arms of chromosome 18 for each of these psychiatric disorders. Some loci are supported by the mapping of chromosome aberrations from psychiatric patients. Mutation analyses of psychiatric patients with 4 candidate genes (NEDD4L, IMPA2, PACAP and GNAL) mapping within these loci have been unsuccessful, although an assocn. was found with the IMPA2 gene in patients with schizophrenia. With these methods and findings, our understanding of the cause of psychiatric disorders assocd. with human chromosome 18 has improved and will advance, esp. with emerging data from the human and rodent genome projects.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:675801 HCAPLUS
DOCUMENT NUMBER: 136:67782
TITLE: Serotonin transporter: From genomics and knockouts to behavioral traits and psychiatric disorders
AUTHOR(S): Lesch, Klaus-Peter
CORPORATE SOURCE: Department of Psychiatry and Psychotherapy, University of Wurzburg, Wurzburg, Germany
SOURCE: Molecular Genetics of Mental Disorders: The Place of Molecular Genetics in Basic Mechanisms and Clinical Applications in Mental Disorders, [Papers presented at an International Symposium], Castres, France, Dec. 1-3, 1999 (2001), Meeting Date 1999, 221-267. Editor(s): Briley, Mike; Sulser, Fridolin. Martin Dunitz Ltd.: London, UK.
CODEN: 69BUOE
DOCUMENT TYPE: Conference; **General Review**

LANGUAGE: English

AB A review discusses the possible role of serotonin transporter gene in the integration of synaptic connections in the mammalian brain during development, adult life, and old age. Allelic variation in functional 5-HTT expression may play a crit. role in synaptic plasticity, thus setting the stage for expression of complex traits and their assocd. behavior throughout adult life. Genetically driven variation of 5-HTT function, in conjunction with other predisposing genetic factors and with inadequate adaptive responses to environmental stressors, is also likely to contribute to the etiopathogenesis and treatment response of affective spectrum disorders emerging from compromised brain development and from neuroadaptive processes.

REFERENCE COUNT: 173 THERE ARE 173 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:483884 HCAPLUS
DOCUMENT NUMBER: 136:132313
TITLE: The effects of tryptophan depletion on mood and psychiatric symptoms
AUTHOR(S): Van der Does, A. J. W.
CORPORATE SOURCE: Departments of Psychology and Psychiatry, Leiden University, Leiden, 2333 AK, Neth.
SOURCE: Journal of Affective Disorders (2001), 64(2-3), 107-119
CODEN: JADID7; ISSN: 0165-0327
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. The no. of studies using Trp depletion (TD) challenge has increased markedly in the past few years. Recently, a no. of neg. results were published, implicating that the effect of TD on mood may be less consistent than previously thought. The literature on the mood effects of TD in psychiatric patients and healthy volunteers was reviewed. TD has a mood-lowering effect in subgroups of recovered depressed patients, patients with seasonal **affective disorder** and vulnerable healthy subjects. The mood effect in former patients is of a different quality, however, than the effect in healthy subjects. Some recent neg. studies in depression might be explained by insufficient lowering of plasma Trp levels. Preliminary evidence exists for an effect of TD on bulimia nervosa, **autism**, aggression and substance dependence. Conclusions: The effects of TD on mood may be more consistent than suggested by a no. of recent neg. studies. Response to TD in recovered depressed patients is assocd. with prior treatment. However, even in SSRI-treated patients the relapse rates are not higher than 50-60%, which needs to be explained. The clin. usefulness of the response to TD in recovered patients (prediction of relapse after treatment discontinuation) and in symptomatic patients (prediction of treatment refractoriness) deserves more research attention. Further suggestions for future research include the cognitive effects of TD in recovered depressed patients and the effect of dietary habits on response to TD.

REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:672769 HCAPLUS
DOCUMENT NUMBER: 134:264009
TITLE: Borna disease virus infection of adult and neonatal rats: models for neuropsychiatric disease
AUTHOR(S): Hornig, Mady; Weissenbock, Herbert; Horscroft, Nigel; O'Rourke, Lisa M.; Lipkin, W. Ian
CORPORATE SOURCE: Emerging Diseases Laboratory, Department of Neurology, College of Medicine, University of California, Irvine, USA
SOURCE: Advances in Animal Virology, Papers presented at the ICGEB-UCI Virology Symposium, 2nd, New Delhi, India, Nov. 9-11, 1998 (2000), Meeting Date 1998, 171-186. Editor(s): Jameel, Shahid; Villarreal, Luis P. Science Publishers, Inc.: Enfield, N. H.
CODEN: 69AKWL
DOCUMENT TYPE: Conference; **General Review**
LANGUAGE: English
AB A review with 76 refs. regarding the establishment of a new animal model for disorders of monoamine circuitry such as **autism**, schizophrenia, and **affective disorders** based on persistent viral infection. This model demonstrates that the manifestations of infection are dependent upon complex interactions between the infectious agent and the host. Crit. features in detg. the nature of disease are the status of the immune system, and the relative maturity of the central nervous system.
REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:675206 HCAPLUS
DOCUMENT NUMBER: 132:145966
TITLE: Psychopharmacology in **autism**
AUTHOR(S): Tsai, Luke Y.
CORPORATE SOURCE: University of Michigan Medical School and Developmental Disorders Clinic, University of Michigan Medical Center, Child and Adolescent Psychiatric Hospital, Ann Arbor, MI, 48109-0390, USA
SOURCE: Psychosomatic Medicine (1999), 61(5), 651-665
CODEN: PSMEAP; ISSN: 0033-3174
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 122 refs. **Autism** is a neurobiol. disorder. The core clin. features of **autism** include impairment in social interaction, impairments in verbal and nonverbal communication, and restricted, repetitive, and stereotyped patterns of behavior, interests, and activities. **Autism** often has coexisting neuropsychiatric disorders, including seizure disorders, attention deficit hyperactivity disorder, **affective disorders**, anxiety disorder, obsessive-compulsive disorder, and Tourette disorder. No etiol.-based treatment modality has been developed to cure individuals with **autism**. However, comprehensive intervention, including parental counseling, behavior modification, special education in a highly structured environment, sensory integration training, speech therapy, social skill training, and medication, has demonstrated significant treatment effects in many individuals with **autism**. Findings from preliminary studies of major neurotransmitters and other neurochem. agents strongly suggest that neurochem. factors play a major role in **autism**. The findings also provide the rationale for psychopharmacotherapy in individuals with **autism**. This article reviews

studies of neurochem. systems and related psychopharmacol. research in **autism** and related neuropsychiatric disorders. Clin. indications for pharmacotherapy are described, and uses of various medications are suggested. This article also discusses new avenues of investigation that may lead to the development of more effective medication treatments in persons with **autism**.

REFERENCE COUNT: 122 THERE ARE 122 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1993:557120 HCAPLUS
DOCUMENT NUMBER: 119:157120
TITLE: Genes with triplet repeats: candidate mediators of neuropsychiatric disorders
AUTHOR(S): Ross, Christopher A.; McInnis, Melvin G.; Margolis, Russell L.; Li, Shi Hua
CORPORATE SOURCE: Sch. Med., Johns Hopkins Univ., Baltimore, MD, 21205-2196, USA
SOURCE: Trends in Neurosciences (1993), 16(7), 254-60
CODEN: TNSCDR; ISSN: 0166-2236
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 90 refs. on the diseases of fragile X syndrome, spinal and bulbar muscle atrophy, myotonic dystrophy and the diseases of fragile Huntington's disease. Three are characterized by unusual patterns of inheritance, in particular, genetic anticipation in which the severity of the disorder increases and the age of onset decreases in successive generations of a pedigree. Several idiopathic neuropsychiatric disorders have features of inheritance consistent with anticipation. In bipolar **affective disorder**, there is evidence for both earlier age of onset and more severe illness in the second generation of a subset of unilineal pedigrees. There is also the suggestion of anticipation in some forms of schizophrenia, spinocerebellar atrophy and **autism**. Triplet repeats are present in addnl. known genes, both in coding regions and untranslated regions. Furthermore, many novel genes with triplet repeats are expressed in the human brain, and these are candidates to cause some forms of these neuropsychiatric disorders.

L3 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1992:56382 HCAPLUS
DOCUMENT NUMBER: 116:56382
TITLE: The opioid model in psychiatric research
AUTHOR(S): Frecska, Ede; Davis, Kenneth L.
CORPORATE SOURCE: Dep. Psychiatry, Mount Sinai Med. Cent., New York, NY, USA
SOURCE: Progress in Psychiatry (1991), 29(Neuropept. Psychiatr. Disord.), 169-91
CODEN: PPSHED; ISSN: 1070-1443
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with ~100 refs. of endogenous opioid peptides role in schizophrenia, **affective disorders**, childhood **autism** and self-injurious behavior, and eating disorders.

```
=> s cerebral () function () disorder?
         91771 CEREBRAL
       1339312 FUNCTION
        416929 FUNCTIONS
       1614475 FUNCTION
                 (FUNCTION OR FUNCTIONS)
        409471 DISORDER?
L4          15 CEREBRAL (W) FUNCTION (W) DISORDER?

=> s l4 and autism?
          1297 AUTISM?
L5           1 L4 AND AUTISM?

=> d l5, ibib abs, 1

L5   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
```

Full Text | Citing References

ACCESSION NUMBER: 2002:72805 HCAPLUS
DOCUMENT NUMBER: 136:139829
TITLE: Compositions comprising sibutramine metabolites in combination with phosphodiesterase inhibitors
INVENTOR(S): Jerussi, Thomas P.; Senanayake, Chrisantha H.; Fang, Qun K.
PATENT ASSIGNEE(S): Sepracor, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S. Ser. No. 662,135.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002010198	A1	20020124	US 2001-770663	20010129
US 6476078	B2	20021105		
US 6331571	B1	20011218	US 1999-372158	19990811
EP 1475086	A2	20041110	EP 2004-18454	19990823
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 6339106	B1	20020115	US 2000-662135	20000914
WO 2002060424	A2	20020808	WO 2002-US2040	20020123
WO 2002060424	A3	20030206		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003096792	A1	20030522	US 2002-278097	20021023
US 2003195261	A1	20031016	US 2003-395298	20030325
US 2004067957	A1	20040408	US 2003-665448	20030922
US 2004092481	A1	20040513	US 2003-693980	20031028
US 2004116534	A1	20040617	US 2003-717653	20031121
US 2004162355	A1	20040819	US 2004-769860	20040203
US 2004180857	A1	20040916	US 2004-806415	20040323

PRIORITY APPLN. INFO.:		
	US 1999-372158	A2 19990811
	US 2000-662135	A2 20000914
	US 1998-97665P	P 19980824
	US 1998-99306P	P 19980902
	EP 1999-945137	A3 19990823
	US 1999-409889	A3 19991001
	US 2001-770663	A 20010129
	US 2001-806	A3 20011204
	US 2002-160033	A3 20020604
	US 2002-278097	A3 20021023

AB Methods are disclosed for the treatment and prevention of disorders and conditions such as, but are not limited to: eating disorders; wt. gain; obesity; irritable bowel syndrome; obsessive-compulsive disorders; platelet adhesion; apnea; affective disorders such as attention deficit disorders, depression, and anxiety; male and female sexual function disorders; restless leg syndrome; osteoarthritis; substance abuse including nicotine and cocaine addiction; narcolepsy; pain such as neuropathic pain, diabetic neuropathy, and chronic pain; migraines; **cerebral function disorders**; chronic disorders such as premenstrual syndrome; and incontinence. Pharmaceutical compns. and dosage forms are also disclosed which comprise a racemic or optically pure sibutramine metabolite and an optional drug. Sibutramine free base was prepd. by the reaction of chlorbenzylnitrile dibromopropane in the presence of NaH in DMSO, followed by the treatment of the resulting 1-(4-chlorophenyl)cyclobutanecarbonitrile with isobutylmagnesium bromide and finally treatment with HCHO. The fee base was resolved into the (R) and (S) isomers and converted into their metabolites. Hard gelatin capsules contained racemic or optically pure sibutramine metabolite 5.0, microcryst. cellulose 90.0, pregelatinized starch 100.3, croscarmellose sodium 7.0, and Mg stearate 0.2 mg.

```
=> s venlafaxine () autism?
          1158 VENLAFAXINE
             1 VENLAFAXINES
          1158 VENLAFAXINE
                 (VENLAFAXINE OR VENLAFAXINES)
          1297 AUTISM?
L6           1 VENLAFAXINE (W) AUTISM?

=> s l6 and review/dt
       1873001 REVIEW/DT
L7           0 L6 AND REVIEW/DT

=> d l6, ibib abs, 1

L6   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
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Full Text | Citing References

ACCESSION NUMBER:	2004:1064323 HCAPLUS
DOCUMENT NUMBER:	142:403954
TITLE:	Venlafaxine has modest effects in autistic children
AUTHOR(S):	Niederhofer, Helmut
CORPORATE SOURCE:	Reparto di Pediatria, Regional Hospital of Bolzano, Bolzano, 39100, Italy
SOURCE:	Therapy (2004), 1(1), 87-90 CODEN: THERCR
PUBLISHER:	Future Drugs Ltd.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

```
AB    Objectives: Few controlled psychopharmacol. trials have been conducted in
      autistic children to det. which agents may be effective at alleviating
      assocd. symptoms.  Methods: Fourteen male children (7.1?3.0 years) with
      autistic disorder, diagnosed by ICD-10 criteria, completed a
      placebo-controlled, double-blind crossover trial of venlafaxine (Effexord,
      Wyeth) administered at a dosage of 30 mg daily for 6 wk.  Subjects were
      included in the study if their eye contact and expressive language were
      inadequate for their developmental level.  Subjects had not tolerated or
      responded to other psychopharmacol. treatments (neuroleptics,
      methylphenidate, clonidine or desipramine).  Results: Teacher ratings on
      the Aberrant Behavior Checklist irritability, stereotype and inappropriate
      speech factors were lower during treatment with venlafaxine than during
      treatment with placebo.  Clinician ratings (Children's Psychiatric Rating
      Scale Autism, Anger and Speech Deviance factors; Children's Global
      Assessment Scale; Clin. Global Impressions Efficacy) of videotaped
      sessions were not significantly different between venlafaxine and placebo.
      Discussion: Venlafaxine was modestly effective in the short-term treatment
      of irritability in some children with autistic disorder.
REFERENCE COUNT:          16    THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> s venlafaxine () neurodegenerative () disorder?
          1158 VENLAFAXINE
             1 VENLAFAXINES
          1158 VENLAFAXINE
                 (VENLAFAXINE OR VENLAFAXINES)
         14262 NEURODEGENERATIVE
             1 NEURODEGENERATIVES
         14262 NEURODEGENERATIVE
                 (NEURODEGENERATIVE OR NEURODEGENERATIVES)
        409471 DISORDER?
L8           0 VENLAFAXINE (W) NEURODEGENERATIVE (W) DISORDER?

=> d his

     (FILE 'HOME' ENTERED AT 18:51:56 ON 22 NOV 2005)

     FILE 'REGISTRY' ENTERED AT 18:52:03 ON 22 NOV 2005

     FILE 'HCAPLUS' ENTERED AT 18:52:06 ON 22 NOV 2005
L1          2114 S AFFECTIVE () DISORDER?
L2           599 S L1 AND REVIEW/DT
L3             8 S L2 AND AUTISM
L4            15 S CEREBRAL () FUNCTION () DISORDER?
L5             1 S L4 AND AUTISM?
L6             1 S VENLAFAXINE () AUTISM?
L7             0 S L6 AND REVIEW/DT
L8             0 S VENLAFAXINE () NEURODEGENERATIVE () DISORDER?

=> s central () nervous () system () disorder?
        361421 CENTRAL
            25 CENTRALS
        361444 CENTRAL
                 (CENTRAL OR CENTRALS)
        192233 NERVOUS
       2184797 SYSTEM
       1202882 SYSTEMS
       2965993 SYSTEM
                 (SYSTEM OR SYSTEMS)
```

```
        409471 DISORDER?
L9         814 CENTRAL (W) NERVOUS (W) SYSTEM (W) DISORDER?

=> s l9 () autism?
          1297 AUTISM?
L10          0 L9 (W) AUTISM?

=> s l9 and autism?
          1297 AUTISM?
L11         23 L9 AND AUTISM?

=> s l11 and review/dt
       1873001 REVIEW/DT
L12          1 L11 AND REVIEW/DT

=> d l12, ibib abs, 1

L12  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
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Full Text | Citing References

ACCESSION NUMBER: 2002:532960 HCAPLUS
DOCUMENT NUMBER: 138:82774
TITLE: Aniracetam: its novel therapeutic potential in cerebral dysfunctional disorders based on recent pharmacological discoveries
AUTHOR(S): Nakamura, Kazuo
CORPORATE SOURCE: Clinical PK Laboratory, Department of Product Research, Nippon Roche Research Center, Kamakura, Japan
SOURCE: CNS Drug Reviews (2002), 8(1), 70-89
CODEN: CDREFB; ISSN: 1080-563X
PUBLISHER: Neva Press
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Aniracetam is a pyrrolidinone-type cognition enhancer that has been clin. used in the treatment of behavioral and psychol. symptoms of dementia following stroke and in Alzheimer's disease. New discoveries in the behavioral-pharmacol., biochem. and pharmacokinetics of aniracetam provided new indications for this drug in the treatment of various **central nervous system disorders** or diseases. This article reviews these new findings and describes the effects of aniracetam in various rodent models of mental-function impairment or cerebral dysfunction. Also, several metabolites of aniracetam have been reported to affect learning and memory in animals. It is, therefore, conceivable that major metabolites of aniracetam contribute to its pharmacol. effects. The animal models used in the pharmacol. evaluation of aniracetam included models of hypoattention, hypovigilance-arousal, impulsiveness, hyperactivity, fear and anxiety, depression, impaired rapid-eye-movement sleep, disturbed temporal regulation, behavioral performance, and bladder hyperactivity. These are models of clin. disorders or symptoms that may include personality disorders, anxiety, depression, post-traumatic stress disorder, attention-deficit/hyperactivity disorder, **autism**, neg. symptoms of schizophrenia, and sleep disorders. At present, there is no convincing evidence that the promising effects of aniracetam in the animal models will guarantee its clin. efficacy. It is conceivable, however, that clin. trials will demonstrate beneficial effects of aniracetam in the above disease states. New findings regarding the mechanism of action of aniracetam, its central target sites, and its effects on signal transduction are also discussed.

REFERENCE COUNT: 103 THERE ARE 103 CITED REFERENCES AVAILABLE FOR

THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

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=> s central () nervous () system
        361421 CENTRAL
            25 CENTRALS
        361444 CENTRAL
                 (CENTRAL OR CENTRALS)
        192233 NERVOUS
       2184797 SYSTEM
       1202882 SYSTEMS
       2965993 SYSTEM
                 (SYSTEM OR SYSTEMS)
L13      71440 CENTRAL (W) NERVOUS (W) SYSTEM

=> s l13 and urinary () incontinence?
        121606 URINARY
          3630 INCONTINENCE?
          1109 URINARY (W) INCONTINENCE?
L14         37 L13 AND URINARY (W) INCONTINENCE?

=> s l14 and review/dt
       1873001 REVIEW/DT
L15         10 L14 AND REVIEW/DT

=> d l15, ibib abs, 1-10

L15  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2005 ACS on STN
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Full Text | Citing References

ACCESSION NUMBER: 2005:111657 HCAPLUS
DOCUMENT NUMBER: 142:347866
TITLE: Pharmacology of the lower urinary tract: basis for current and future treatments of **urinary incontinence**
AUTHOR(S): Andersson, Karl-Erik; Wein, Alan J.
CORPORATE SOURCE: Department of Clinical Pharmacology, Lund University Hospital, Lund, Swed.
SOURCE: Pharmacological Reviews (2004), 56(4), 581-631
CODEN: PAREAQ; ISSN: 0031-6997
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. The lower urinary tract constitutes a functional unit controlled by a complex interplay between the central and peripheral nervous systems and local regulatory factors. In the adult, micturition is controlled by a spinobulbospinal reflex, which is under suprapontine control. Several **central nervous system** transmitters can modulate voiding, as well as, potentially, drugs affecting voiding; for example, noradrenaline, GABA, or dopamine receptors and mechanisms may be therapeutically useful. Peripherally, lower urinary tract function is dependent on the concerted action of the smooth and striated muscles of the urinary bladder, urethra, and periurethral region. Various neurotransmitters, including acetylcholine, noradrenaline, ATP, nitric oxide, and neuropeptides, have been implicated in this neural regulation. Muscarinic receptors mediate normal bladder contraction as well as at least the main part of contraction in the overactive bladder. Disorders of micturition can roughly be classified as disturbances of storage or disturbances of emptying. Failure to store urine may lead to various

forms of incontinence, the main forms of which are urge and stress incontinence. The etiol. and pathophysiol. of these disorders remain incompletely known, which is reflected in the fact that current drug treatment includes a relatively small no. of more or less well-documented alternatives. Antimuscarinics are the mainstay of pharmacol. treatment of the overactive bladder syndrome, which is characterized by urgency, frequency, and urge incontinence. Accepted drug treatments of stress incontinence are currently scarce, but new alternatives are emerging. New targets for control of micturition are being defined, but further research is needed to advance the pharmacol. treatment of micturition disorders.

REFERENCE COUNT: 675 THERE ARE 675 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2005:52316 HCAPLUS
DOCUMENT NUMBER: 142:290514
TITLE: Therapeutic strategies for urge **urinary incontinence**
AUTHOR(S): Steers, William D.
CORPORATE SOURCE: Department of Urology, University of Virginia Health System, Charlottesville, VA, 22908, USA
SOURCE: Drug Discovery Today: Therapeutic Strategies (2004), 1(2), 267-273
CODEN: DDTTC6; ISSN: 1740-6773
URL: http://www.sciencedirect.com/science/journal/17406773
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; **General Review**; (online computer file)
LANGUAGE: English

AB A review. **Urinary incontinence** and the related disorder overactive bladder (OAB) arise from diverse etiologies. Current drug therapies are often not curative and are assocd. with prohibitive side effects. New therapeutic strategies will go beyond smooth muscle targets to include visceral afferents and micturition pathways in the **central nervous system** (CNS).

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:644185 HCAPLUS
DOCUMENT NUMBER: 142:16872
TITLE: Targeting serotonin and norepinephrine receptors in stress **urinary incontinence**
AUTHOR(S): Thor, K. B.
CORPORATE SOURCE: Laboratory of Neurourology, Chief Scientific Officer, Dynogen Pharmaceuticals, Inc., Duke University, Durham, NC, USA
SOURCE: International Journal of Gynecology & Obstetrics (2004), 86(Suppl. 1), S38-S52
CODEN: IJGOAL; ISSN: 0020-7292
PUBLISHER: Elsevier Ireland Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Stress **urinary incontinence** (SUI) in women is prevalent, and there are no globally developed or widely approved drugs for the disease. One strategy for improving urinary continence is to augment the

function of the urethral rhabdosphincter through neuropharmacol. The present review describes the innervation of the urethra, and the role of the **central nervous system** in controlling nerve activity. Targeting serotonin and norepinephrine (or noradrenaline) receptors in Onuf's nucleus is shown to augment the function of the urethral rhabdosphincter by increasing pudendal nerve efferent activity. It is proposed that the ability of serotonin and norepinephrine to enhance the effects of glutamate (the primary excitatory neurotransmitter for pudendal sphincter motor neurons) while having no direct effects of their own, allow facilitation of rhabdosphincter activity during urine storage while allowing complete relaxation during micturition. Duloxetine, a potent and balanced dual serotonin (5-HT)-norepinephrine reuptake inhibitor (SNRI), potentiates these physiol. effects of endogenous serotonin and norepinephrine (by inhibiting the reuptake of these neurotransmitters in the pre-synaptic element) and thereby enhances the **central nervous system**'s natural continence control mechanisms.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:479375 HCAPLUS
DOCUMENT NUMBER: 141:167881
TITLE: **Central nervous system** control of the lower urinary tract: new pharmacological approaches to stress **urinary incontinence** in women
AUTHOR(S): Thor, Karl B.; Donatucci, Craig
CORPORATE SOURCE: Dynogen Pharmaceuticals, Inc. and Division of Urology, Department of Surgery, Duke University Medical Center, Durham, NC, USA
SOURCE: Journal of Urology (Hagerstown, MD, United States) (2004), 172(1), 27-33
CODEN: JOURAA; ISSN: 0022-5347
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Despite the prevalence of stress **urinary incontinence** in women there are no approved drugs for the disease. Designing medical therapies requires a comprehensive understanding of how the internal and external sphincters are neurol. controlled. In this review recent advances in mapping storage and micturition reflexes, and the assocn. of serotonergic and noradrenergic systems with these reflexes are discussed. Urine storage and micturition are controlled by a series of hard wired reflexes that are under the modulatory influence of serotonin and norepinephrine. Augmentation of the serotonergic and noradrenergic systems with duloxetine increases bladder capacity and urethral rhabdosphincter activity. The increase in sphincter activity is mediated by α1 adrenergic receptors and 5-hydroxytryptamine receptors. Increasing rhabdosphincter activity with duloxetine may offer a therapeutic benefit in women with stress **urinary incontinence**.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:816821 HCAPLUS
DOCUMENT NUMBER: 139:16859
TITLE: Current and Future Pharmacological Treatment for

Overactive Bladder.
AUTHOR(S): Yoshimura, Naoki; Chancellor, Michael B.
CORPORATE SOURCE: Dep. Urol., Univ. Pittsburgh Sch. Med., Pittsburgh, PA, USA
SOURCE: Journal of Urology (Hagerstown, MD, United States) (2002), 168(5), 1897-1913
CODEN: JOURAA; ISSN: 0022-5347
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. PURPOSE: **Urinary incontinence** and overactive bladder are important and common conditions that have received little general medical attention. The authors reviewed the magnitude and impact of these conditions, and discuss pharmacotherapy as well as new drugs under investigation. MATERIALS AND METHODS: The main emphasis of this review is pharmacol. therapy for the bladder. The authors discuss currently available agents, drugs under development and pharmacol. targets that would be suitable targets for treating overactive bladder. Drugs such as duloxetine that target not bladder smooth muscle, but rather **central nervous system** control of the micturition reflex are undergoing clin. trials. The authors also discuss intravesical therapy and alternative drug delivery methods, such as intravesical capsaicin and botulinum toxin, with special emphasis on approaches to modulate bladder afferent nerve function for preventing overactive bladder. RESULTS: There are many advantages to advanced drug delivery systems, including long-term therapeutic efficacy, decreased side effects and improved patient compliance. Future speculation such as gene therapy holds great promise for overactive bladder because it is possible to access all genitourinary organs via endoscopy and other minimally invasive techniques that are ideally suited for gene therapy. CONCLUSIONS: Traditional anticholinergic therapies are limited in their effectiveness. There is great hope for future research regarding voiding dysfunction and **urinary incontinence** through a focus on afferent nerve intervention for preventing overactive bladder.
REFERENCE COUNT: 176 THERE ARE 176 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2002:764183 HCAPLUS
DOCUMENT NUMBER: 138:296900
TITLE: Pharmacology and potential therapeutic applications of nitric oxide-releasing nonsteroidal anti-inflammatory and related nitric oxide-donating drugs
AUTHOR(S): Keeble, J. E.; Moore, P. K.
CORPORATE SOURCE: Centre for Cardiovascular Biology and Medicine, King's College, University of London, London, SE1 9RT, UK
SOURCE: British Journal of Pharmacology (2002), 137(3), 295-310
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review examg. the biol. significance, therapeutic potential and mechanism(s) of action of a range of NO-releasing nonsteroidal anti-inflammatory drugs (NO-NSAIDs) and related NO-donating drugs (NODDs) that are not NSAIDs. The slow release of NO from these compds. leads to subtle changes in the profile of pharmacol. activity of the std. NSAIDs.

For example, compared with NSAIDs, NO-NSAIDs have markedly diminished gastrointestinal toxicity and improved anti-inflammatory and antinociceptive efficacy. In addn., nitroparacetamol exhibits hepatoprotection as opposed to the hepatotoxic activity of paracetamol. The possibility that NO-NSAIDs or NODDs may be of therapeutic benefit in a wide variety of disease states, including pain and inflammation, thrombosis and restenosis, neurodegenerative diseases of the **central nervous system**, colitis, cancer, **urinary incontinence**, liver disease, impotence, bronchial asthma and osteoporosis, is discussed.

REFERENCE COUNT: 145 THERE ARE 145 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:623231 HCAPLUS
DOCUMENT NUMBER: 137:179283
TITLE: The tolerability and safety of cholinesterase inhibitors in the treatment of dementia
AUTHOR(S): Inglis, F.
CORPORATE SOURCE: Glasgow Memory Clinic, Clydebank, UK
SOURCE: International Journal of Clinical Practice, Supplement (2002), 127, 45-63
CODEN: ICPSFY; ISSN: 1368-504X
PUBLISHER: Medicom International
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Cholinesterase inhibitors (ChEIs) are dosed in two phases for the treatment of dementia, an initial dose-escalation phase to achieve a therapeutic dose and a maintenance phase where the therapeutic dose is given for long-term therapy. ChEIs are assocd. with a range of side effects as a result of cholinergic stimulation in different areas of the brain and the periphery. Acute, centrally-mediated gastrointestinal events (mostly nausea and vomiting) are class effects of all ChEIs, and are reported mostly during the dose-escalation phase of therapy. These events have been assocd. more with the dual acetylcholinesterase/butyrylch olinesterase (AChE/BuChE) inhibitor rivastigmine than with the AChE-selective inhibitors donepezil and galantamine, probably due to rivastigmine's higher potency. However, these events can be minimized using slow dose escalation with small dose graduations and administration with food. Other side effects assocd. with ChEIs include **central nervous system** events, extrapyramidal symptoms, sleep disturbances and cardiorespiratory events, assocd. with cholinergic activity in the cortex, caudate nucleus, brainstem and medulla, resp., and muscle cramps and weakness, cardiorespiratory events and **urinary incontinence**, assocd. with peripheral cholinergic activity. These symptoms are mostly reported during the maintenance phase of therapy. They are more frequently reported with donepezil, but are rarely reported with rivastigmine, and galantamine may not have been marketed long enough to make an adequate assessment. These differences are due to the drugs' resp. pharmacol. For example, donepezil and rivastigmine are active centrally, in contrast to galantamine, which is more active peripherally. Furthermore, rivastigmine preferentially inhibits the G1 isoform of cholinesterase, predominantly located in the cortex, hippocampus and in neuritic plaques, while donepezil and galantamine are not selective for any cholinesterase isoforms and have wide cholinergic activity both centrally and peripherally. The cholinergic activity of rivastigmine, in contrast to donepezil and galantamine, is apparently more targeted at clin. relevant brain sites. The pharmacol. profile of rivastigmine results in it having

a low potential to interact with other drugs and it may be used with a high margin of safety in patients having a wide variety of concomitant diseases. Donepezil and galantamine may have significant interactions with other drugs that are metabolized by the hepatic cytochrome system and therefore need to be used with caution in patients with many concomitant illnesses. When dosed with care, ChEIs are well tolerated and patient compliance and patient and caregiver acceptability are good. The favorable tolerability and safety profiles of these agents make them suitable first-line therapy for dementia. In addn., patients who have tolerability and/or safety problems in maintenance treatment that limit the use of donepezil or galantamine may benefit from switching to rivastigmine.

REFERENCE COUNT: 129 THERE ARE 129 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:38831 HCAPLUS
DOCUMENT NUMBER: 137:3845
TITLE: Depression and incontinence
AUTHOR(S): Steers, William D.; Lee, Kyu-Sung
CORPORATE SOURCE: Department of Urology, University of Virginia Health Sciences Center, University of Virginia School of Medicine, Charlottesville, VA, 22908, USA
SOURCE: World Journal of Urology (2001), 19(5), 351-357
CODEN: WJURDJ; ISSN: 0724-4983
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. The urol. literature suggests that there is an assocn. between a variety of psychiatric disorders and incontinence. Most notably, depression is found in a significant percentage of patients with **urinary incontinence**. Depression also occurs in other conditions assocd. with urinary urge incontinence, such as aging and dementia, and in neurol. disorders such as normal pressure hydrocephalus. Correction of some neurol. disorders eliminates both depression and urge incontinence. Although chronic medical disorders such as urge incontinence may lead to depression, an alternative hypothesis is that these 2 conditions share a common neurochem. pathogenesis. Lowering monoamines such as serotonin and noradrenaline in the **central nervous system** (CNS) leads to depression and urinary frequency and a hyperactive bladder in exptl. animals. Thus, depression may not only be the result of persistent **urinary incontinence**, but individuals with altered CNS monoamines could manifest both depression and an overactive bladder. The latter condition may lead to urge incontinence, urinary frequency, urgency, or enuresis. Uncovering further evidence for such a linkage could serve as the basis for the development of genetic markers and novel therapeutic interventions for these 2 conditions.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:697822 HCAPLUS
DOCUMENT NUMBER: 136:363091
TITLE: Vanilloid receptor ligands: Hopes and realities for the future

AUTHOR(S): Szallasi, Arpad
CORPORATE SOURCE: Department of Pathology and Immunology, Washington University School of Medicine, St Louis, MO, USA
SOURCE: Drugs & Aging (2001), 18(8), 561-573
CODEN: DRAGE6; ISSN: 1170-229X
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Neurons possessing C-fibers transmit nociceptive information into the **central nervous system** and participate in various reflex responses. These neurons carry receptors that bind capsaicin, recently identified as the vanilloid VR1 receptor. Excitation of these cells by capsaicin is followed by a lasting refractory state, termed desensitization, in which the neurons fail to respond to a variety of noxious stimuli. Desensitization to capsaicin has a clear therapeutic potential in relieving neuropathic pain and ameliorating urinary bladder overactivity, just to cite 2 important examples. Vanilloids may also be beneficial in the treatment of benign prostate hyperplasia (BPH). Since the majority of elderly patients have neuropathic pain co-existent with **urinary incontinence** and/or BPH, a drug that ameliorates pain and improves urinary symptoms at the same time promises to be of great clin. value in geriatric medicine. In fact, capsaicin has already been shown to have a role in the treatment of conditions that can arise in the elderly, including herpes zoster-related neuropathic pain, diabetic neuropathy, postmastectomy pain, uremic itching assocd. with renal failure, and **urinary incontinence**. The potent VR1 agonist resiniferatoxin, now in phase II clin. trials, appears to be superior to capsaicin in terms of its tolerability profile. Recent discoveries enhance the therapeutic potential of vanilloids. The recognition that VR1 also functions as a principal receptor for protons and eicosanoids implies that VR1 antagonists may be of value in the treatment of inflammatory hyperalgesia and pain. Animal experimentation has already lent support to this assumption. The discovery of VR1-expressing cells in the brain as well as in non-neural tissues such as the kidney and urothelium places VR1 in a much broader perspective than peripheral pain perception, and is hoped to identify further, yet unsuspected, indications for vanilloid therapy. The realization that VR1 and cannabinoid CB1 receptors have overlapping ligand recognition properties may also have far-reaching implications for vanilloid therapy. In fact, arvanil, a combined agonist of VR1 and CB1 receptors, has already proved to be a powerful analgesic drug in the mouse. From academic mol. biol. labs. to industrial drug discovery centers to the clinics, there is a steady flow of new data, forcing us to constantly revise the ways the authors are thinking about vanilloid receptor ligands and their hopes and realities for the future. This review covers the most promising current trends in vanilloid research with special emphasis on geriatric medicine.

REFERENCE COUNT: 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Cited References

ACCESSION NUMBER: 2001:525684 HCAPLUS
DOCUMENT NUMBER: 135:237682
TITLE: Carbon monoxide poisoning: Systemic manifestations and complications
AUTHOR(S): Choi, Il Saing
CORPORATE SOURCE: Department of Neurology, Yonsei University College of Medicine, Seoul, 120-752, S. Korea
SOURCE: Journal of Korean Medical Science (2001), 16(3),

253-261
CODEN: JKMSEH; ISSN: 1011-8934
PUBLISHER: Korean Academy of Medical Science
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review and discussion with 140 refs. CO has the toxic effects of tissue hypoxia and produces various systemic and neurol. complications. The main clin. manifestations of acute CO poisoning consist of symptoms caused by alterations of the cardiovascular system such as initial tachycardia and hypertension, and **central nervous system** symptoms such as headache, dizziness, paresis, convulsion, and unconsciousness. CO poisoning also produces myocardial ischemia, atrial fibrillation, pneumonia, pulmonary edema, erythrocytosis, leukocytosis, hyperglycemia, muscle necrosis, acute renal failure, skin lesion, and changes in perception of the visual and auditory systems. Of considerable clin. interest, severe neurol. manifestations may occur days or weeks after acute CO poisoning. Delayed sequelae of CO poisoning are not rare, usually occur in middle or older, and are clin. characterized by the symptom triad of mental deterioration, **urinary incontinence**, and gait disturbance. Occasionally, movement disorders, particularly parkinsonism, are obsd. In addn., peripheral neuropathy following CO poisoning usually occurs in young adults.

REFERENCE COUNT: 140 THERE ARE 140 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s l13 () chronic () obstructive () pulmonary () disease?
        187986 CHRONIC
             6 CHRONICS
        187990 CHRONIC
                 (CHRONIC OR CHRONICS)
          9687 OBSTRUCTIVE
             1 OBSTRUCTIVES
          9688 OBSTRUCTIVE
                 (OBSTRUCTIVE OR OBSTRUCTIVES)
         75703 PULMONARY
             2 PULMONARIES
         75703 PULMONARY
                 (PULMONARY OR PULMONARIES)
        918183 DISEASE?
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=> s venlafaxine () post () traumatic () stress
L1 0 VENLAFAXINE (W) POST (W) TRAUMATIC (W) STRESS

=> s venlafaxine? () derivative?
L2 7 VENLAFAXINE? (W) DERIVATIVE?

=> d l2

L2 ANSWER 1 OF 7 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
Full Text | Citing References
AN 2002:171133 BIOSIS
DN PREV200200171133
TI Derivatives of (-)-venlafaxine and methods of preparing and using the same.
AU Jerussi, Thomas P. [Inventor]; Senanayake, Chrisantha H. [Inventor]
CS ASSIGNEE: Sepracor, Inc.
PI US 6342533 20020129

SO Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 29, 2002) Vol. 1254, No. 5. http://www.uspto.gov/web/menu/patdata.html. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DT Patent
LA English
ED Entered STN: 5 Mar 2002
Last Updated on STN: 4 Apr 2002

=> d l2, ibib abs, 1-2

L2 ANSWER 1 OF 7 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
Full Text | Chira References

ACCESSION NUMBER: 2002:171133 BIOSIS
DOCUMENT NUMBER: PREV200200171133
TITLE: Derivatives of (-)-venlafaxine and methods of preparing and using the same.
AUTHOR(S): Jerussi, Thomas P. [Inventor]; Senanayake, Chrisantha H. [Inventor]
CORPORATE SOURCE: ASSIGNEE: Sepracor, Inc.
PATENT INFORMATION: US 6342533 20020129
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 29, 2002) Vol. 1254, No. 5. http://www.uspto.gov/web/menu/patdata.html. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Mar 2002
Last Updated on STN: 4 Apr 2002

1020

AB Methods of preparing, and compositions comprising, derivatives of (-)-venlafaxine are disclosed. Also disclosed are methods of treating and preventing diseases and disorders including, but not limited to, affective disorders such as depression, bipolar and manic disorders, attention deficit disorder, attention deficit disorder with hyperactivity, Parkinson's disease, epilepsy, cerebral function disorders, obesity and weight gain, incontinence, dementia and related disorders.

L2 ANSWER 2 OF 7 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
Full Text | Chira References

ACCESSION NUMBER: 2001:391812 BIOSIS
DOCUMENT NUMBER: PREV200100391812
TITLE: Derivatives of (+)-venlafaxine and methods of preparing and using the same.
AUTHOR(S): Jerussi, Thomas P. [Inventor]; Senanayake, Chrisantha H. [Inventor, Reprint author]
CORPORATE SOURCE: Shrewsbury, MA, USA
ASSIGNEE: Sepracor, Inc.
PATENT INFORMATION: US 6197828 20010306
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Mar. 6, 2001) Vol. 1244, No. 1. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Aug 2001
Last Updated on STN: 23 Feb 2002

AB Methods of preparing, and compositions comprising, derivatives of (+)-venlafaxine are disclosed. Also disclosed are methods of treating and

preventing diseases and disorders including, but not limited to, affective disorders such as depression, bipolar and manic disorders, attention deficit disorder, attention deficit disorder with hyperactivity, Parkinson's disease, epilepsy, cerebral function disorders, obesity and weight gain, incontinence, dementia and related disorders.

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     (FILE 'HOME' ENTERED AT 12:05:34 ON 22 NOV 2005)

     FILE 'REGISTRY' ENTERED AT 12:09:17 ON 22 NOV 2005

     FILE 'MEDLINE, BIOSIS, EMBASE, HCAPLUS' ENTERED AT 12:09:40 ON 22 NOV 2005
L1            0 S VENLAFAXINE () POST () TRAUMATIC () STRESS
L2            7 S VENLAFAXINE? () DERIVATIVE?

=> s venlafaxine () analog?
L3            1 VENLAFAXINE (W) ANALOG?

=> d l3, ibib abs, 1

L3   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
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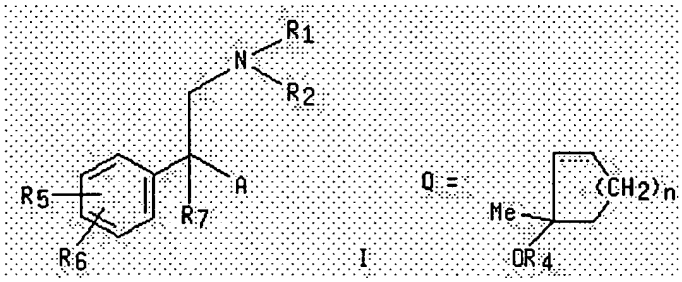
Full Text | Citing References

ACCESSION NUMBER: 1996:275079 HCAPLUS
DOCUMENT NUMBER: 124:333103
TITLE: Venlafaxine and related compounds for the treatment of hypothalamic amenorrhea in nondepressed women
INVENTOR(S): Upton, Gertrude V.; Derivan, Albert T.; Rudolph, Richard L.
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5506270	A	19960409	US 1995-380903	19950130
EP 723779	A1	19960731	EP 1995-309169	19951218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
NZ 280744	A	20001124	NZ 1995-280744	19951221
ZA 9511038	A	19970630	ZA 1995-11038	19951228
FI 9506339	A	19960731	FI 1995-6339	19951229
NO 9505356	A	19960731	NO 1995-5356	19951229
AU 9540752	A1	19960808	AU 1995-40752	19951229
AU 703529	B2	19990325		
HU 75095	A2	19970428	HU 1995-3922	19951229
CA 2167999	AA	19960731	CA 1996-2167999	19960124
JP 08231387	A2	19960910	JP 1996-10850	19960125
CN 1137894	A	19961218	CN 1996-105561	19960129
PRIORITY APPLN. INFO.:			US 1995-380903 A	19950130

OTHER SOURCE(S): MARPAT 124:333103
GI



AB A method is provided for treating hypothalamic amenorrhea in a nondepressed female mammal by administering to the mammal an effective amt. of a hydroxycycloalkanephenethyl amine compd. I (A = Q; dotted line = optional unsatn.; R1, R7 = H, alkyl; R2 = alkyl; R4 = H, alkyl, formyl, alkanol; R5, R6 = H, OH, alkyl, alkoxy, alkanoyloxy, cyano, nitro, alkylmercapto, amino, alkylamino, dialkylamino, alkanamido, halo, trifluoromethyl, or, taken together, methylene dioxy; n = 0-4) or a pharmaceutically acceptable salt thereof. Of particular interest are venlafaxine and its pharmaceutically acceptable salts.

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     FILE 'REGISTRY' ENTERED AT 12:09:17 ON 22 NOV 2005

     FILE 'MEDLINE, BIOSIS, EMBASE, HCAPLUS' ENTERED AT 12:09:40 ON 22 NOV 2005
L1            0 S VENLAFAXINE () POST () TRAUMATIC () STRESS
L2            7 S VENLAFAXINE? () DERIVATIVE?
L3            1 S VENLAFAXINE () ANALOG?

=> s l2 and review/dt
L4            0 L2 AND REVIEW/DT

=> s venlafaxine?
L5         8967 VENLAFAXINE?

=> s senile () dementia or Parkinson's () disease? or epilepsy? or Alzheimer? () dis
MISMATCHED QUOTE 'PARKINSON'S'
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting
off or masking.

=> s senile () dementia? or Parkinson? () disease? or epilepsy? or Alzheimer? () dis
L6       626478 SENILE (W) DEMENTIA? OR PARKINSON? (W) DISEASE? OR EPILEPSY? OR
                ALZHEIMER? (W) DISEASE? OR AMNESIA? OR AMNESIC (W) SYNDROME? OR
                SHY? (W) SYNDROME? OR ANXIETY?

=> s l6 ()  l5
L7           12 L6 (W) L5

=> s l7 and review/dt
L8            1 L7 AND REVIEW/DT

=> d l8, ibib abs, 1

L8   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
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Full Text | Citing References

ACCESSION NUMBER: 2000:14375 HCAPLUS
DOCUMENT NUMBER: 132:44393
TITLE: Venlafaxine extended release (XR) in the treatment of generalized anxiety disorder
AUTHOR(S): Sheehan, David V.
CORPORATE SOURCE: Institute for Research in Psychiatry, The University of South Florida, Tampa, FL, USA
SOURCE: Journal of Clinical Psychiatry (1999), 60(Suppl. 22), 23-28
CODEN: JCLPDE; ISSN: 0160-6689
PUBLISHER: Physicians Postgraduate Press, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 26 refs. This article reviews results of reports suggesting that venlafaxine extended release (XR) may play an important role in the treatment of anxiety disorders, particularly generalized anxiety disorder (GAD). Statistically significant improvements in GAD for venlafaxine XR compared with placebo on the basis of the Hamilton Rating Scale for Anxiety were seen in the acute treatment studies up to 8 wk and were maintained for 6 mo. One comparative study found venlafaxine XR to be as effective as, or on some measures more effective than, buspirone at relieving GAD. Venlafaxine XR was safe and well tolerated in the GAD studies, with discontinuation rates due to adverse effects similar to the rates seen with placebo or buspirone.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s schizophrenia or borderline () personality () disorder?
L9 187794 SCHIZOPHRENIA OR BORDERLINE (W) PERSONALITY (W) DISORDER?

=> d his

(FILE 'HOME' ENTERED AT 12:05:34 ON 22 NOV 2005)

FILE 'REGISTRY' ENTERED AT 12:09:17 ON 22 NOV 2005

FILE 'MEDLINE, BIOSIS, EMBASE, HCAPLUS' ENTERED AT 12:09:40 ON 22 NOV 2005
L1 0 S VENLAFAXINE () POST () TRAUMATIC () STRESS
L2 7 S VENLAFAXINE? () DERIVATIVE?
L3 1 S VENLAFAXINE () ANALOG?
L4 0 S L2 AND REVIEW/DT
L5 8967 S VENLAFAXINE?
L6 626478 S SENILE () DEMENTIA? OR PARKINSON? () DISEASE? OR EPILEPSY? OR
L7 12 S L6 () L5
L8 1 S L7 AND REVIEW/DT
L9 187794 S SCHIZOPHRENIA OR BORDERLINE () PERSONALITY () DISORDER?

=> s l9 () l5
L10 1 L9 (W) L5

=> s l10 and review/dt
L11 0 L10 AND REVIEW/DT

=> s cocaine () addiction or alcohol () addiction?
L12 4026 COCAINE (W) ADDICTION OR ALCOHOL (W) ADDICTION?

=> s l12 () l5
L13 0 L12 (W) L5

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=> s l12 and l5
L14           9 L12 AND L5

=> s l14 and review/dt
L15           0 L14 AND REVIEW/DT

=> s bulimia () nervosa? or Gilles? () tourette () syndrome or vasomotor () flushing
L16       16028 BULIMIA (W) NERVOSA? OR GILLES? (W) TOURETTE (W) SYNDROME OR
                VASOMOTOR (W) FLUSHING? OR CHRONIC (W) FATIGUE (W) SYNDROME?

=> s l16 () l5
L17           0 L16 (W) L5

=> s l16 and l5
L18          66 L16 AND L5

=> s l18 and review/dt
L19           4 L18 AND REVIEW/DT

=> d l19, ibib abs, 1-4

L19  ANSWER 1 OF 4     MEDLINE on STN
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Full Text | Citing References

ACCESSION NUMBER: 2003366271 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12900988
TITLE: Pharmacologic treatment of binge eating disorder.
AUTHOR: Carter William P; Hudson James I; Lalonde Justine K; Pindyck Lindsay; McElroy Susan L; Pope Harrison G Jr
CORPORATE SOURCE: Biological Psychiatry Laboratory, McLean Hospital, Belmont, MA 02478, USA.. wpcarter@partners.org
CONTRACT NUMBER: T32 DA 07252 (NIDA)
SOURCE: International journal of eating disorders, (2003) 34 Suppl S74-88. Ref: 50
Journal code: 8111226. ISSN: 0276-3478.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20030806
Last Updated on STN: 20031224
Entered Medline: 20031223

AB OBJECTIVE: To review the findings from pharmacologic trials of binge eating disorder (BED) and to provide guidelines for pharmacologic treatment. METHODS: The literature was searched for studies of pharmacologic treatment of BED and related conditions, such as nonpurging **bulimia nervosa**. RESULTS: Placebo-controlled studies of desipramine, fluvoxamine, fluoxetine, sertraline, citalopram, dexfenfluramine, sibutramine, and topiramate have demonstrated the efficacy of these agents in the treatment of BED. An open trial of **venlafaxine** has offered preliminary evidence for the efficacy of this medication. Guidelines for pharmacologic management of BED are provided. CONCLUSIONS: The literature offers support for the use of agents from three categories of medication (antidepressants, appetite suppressants, and anticonvulsants) in the treatment of BED.

L19 ANSWER 2 OF 4 MEDLINE on STN

Full Text | Citing References

ACCESSION NUMBER: 2000387069 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10926050
TITLE: New indications for antidepressants.
COMMENT: Comment in: J Clin Psychiatry. 2001 Oct;62(10):829-30.
PubMed ID: 11816876
AUTHOR: Schatzberg A F
CORPORATE SOURCE: Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Calif 94305-5548, USA.
SOURCE: Journal of clinical psychiatry, (2000) 61 Suppl 11 9-17.
Ref: 73
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000818
Last Updated on STN: 20020426
Entered Medline: 20000804

AB The second and third generation of antidepressants, i.e., the selective serotonin reuptake inhibitors, nefazodone, **venlafaxine**, and mirtazapine, are proving to be useful in a variety of seemingly diverse disorders, including most anxiety disorders. In addition to receiving approval from the U.S. Food and Drug Administration (FDA) for major depressive disorder, some of the newer antidepressants have received FDA approval for other disorders, e.g., generalized anxiety disorder (**venlafaxine**), **bulimia nervosa** (fluoxetine), obsessive-compulsive disorder (fluvoxamine, paroxetine, sertraline, and fluoxetine), social phobia (paroxetine), panic disorder (sertraline, paroxetine), and posttraumatic stress disorder (sertraline). In controlled studies, these agents have also shown usefulness in premenstrual dysphoric disorder, borderline personality disorder, obesity, smoking cessation, and alcoholism. This article describes the new and potential indications for recently developed antidepressants and the studies that suggested these indications.

L19 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:596373 HCAPLUS
DOCUMENT NUMBER: 134:65678
TITLE: New indications for antidepressants
AUTHOR(S): Schatzberg, Alan F.
CORPORATE SOURCE: Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA, 94305-5548, USA
SOURCE: Journal of Clinical Psychiatry (2000), 61(Suppl. 11), 9-17
CODEN: JCLPDE; ISSN: 0160-6689
PUBLISHER: Physicians Postgraduate Press, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 73 refs. The second and third generation of antidepressants, i.e., the selective serotonin reuptake inhibitors, nefazodone, **venlafaxine**, and mirtazapine, are proving to be useful in a variety of seemingly diverse disorders, including most anxiety disorders. In addn. to receiving approval from the U.S. Food and Drug Administration.

(FDA) for major depressive disorder, some of the newer antidepressants have received FDA approval for other disorders, e.g., generalized anxiety disorder (**venlafaxine**), **bulimia nervosa** (fluoxetine), obsessive-compulsive disorder (fluvoxamine, paroxetine, sertraline, and fluoxetine), social phobia (paroxetine), panic disorder (sertraline, paroxetine), and posttraumatic stress disorder (sertraline). In controlled studies, these agents have also shown usefulness in premenstrual dysphoric disorder, borderline personality disorder, obesity, smoking cessation, and alcoholism. This article describes the new and potential indications for recently developed antidepressants and the studies that suggested these indications.

REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:469364 HCAPLUS
DOCUMENT NUMBER: 129:239318
TITLE: Potential applications of **venlafaxine**
AUTHOR(S): Nutt, D.; Johnson, F. Neil
CORPORATE SOURCE: School of Medical Sciences, University of Bristol, Bristol, BS8 1TD, UK
SOURCE: Reviews in Contemporary Pharmacotherapy (1998), 9(5), 321-331
CODEN: RCPHFW; ISSN: 0954-8602
PUBLISHER: Marius Press
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 95 refs. The action of **venlafaxine** on at least two neurotransmitter systems suggests that this agent may have potential applications in a variety of conditions in addn. to the treatment of depression. Evidence on the point is relatively scanty at the present time, but such information as is available suggests that **venlafaxine** may have a future role in the management of several psychiatric conditions. These include: obsessive-compulsive disorder; panic disorder; attention deficit hyper-activity disorder (in children and in adults); borderline personality disorder; **chronic fatigue syndrome**; and possibly loss of libido and/or erectile dysfunction. There are also suggestions of therapeutic benefit arising from **venlafaxine** treatment of phobic conditions, specifically agoraphobia and social phobia. Recent work indicates that **venlafaxine** may reduce anxiety concomitant with depressive symptoms as well as anxiety occurring in the absence of depression, and that it may be rather more effective in doing so than is the case for several comparator agents. **Venlafaxine** appears to be effective in treating certain forms of pain; this is particularly evident against some types of headache, and there are indications of efficacy also against postherpetic neuralgia, chronic radicular back pain, and fibromyalgia. While **venlafaxine** has been found to show some degree of efficacy against Raynaud's phenomenon, it is unlikely to be better than selective serotonin reuptake inhibitors in the treatment of this condition. Further studies of **venlafaxine** are likely to reveal a wider spectrum of potential applications for this agent.

REFERENCE COUNT: 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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     FILE 'REGISTRY' ENTERED AT 12:09:17 ON 22 NOV 2005

     FILE 'MEDLINE, BIOSIS, EMBASE, HCAPLUS' ENTERED AT 12:09:40 ON 22 NOV 2005
L1             0 S VENLAFAXINE () POST () TRAUMATIC () STRESS
L2             7 S VENLAFAXINE? () DERIVATIVE?
L3             1 S VENLAFAXINE () ANALOG?
L4             0 S L2 AND REVIEW/DT
L5          8967 S VENLAFAXINE?
L6        626478 S SENILE () DEMENTIA? OR PARKINSON? () DISEASE? OR EPILEPSY? OR
L7            12 S L6 ()  L5
L8             1 S L7 AND REVIEW/DT
L9        187794 S SCHIZOPHRENIA OR BORDERLINE () PERSONALITY () DISORDER?
L10            1 S L9 () L5
L11            0 S L10 AND REVIEW/DT
L12         4026 S COCAINE () ADDICTION OR ALCOHOL () ADDICTION?
L13            0 S L12 () L5
L14            9 S L12 AND L5
L15            0 S L14 AND REVIEW/DT
L16        16028 S BULIMIA () NERVOSA? OR GILLES? () TOURETTE () SYNDROME OR VAS
L17            0 S L16 () L5
L18           66 S L16 AND L5
L19            4 S L18 AND REVIEW/DT

=> s l5 and urinary () incontinence?
L20           36 L5 AND URINARY (W) INCONTINENCE?

=> a l20 and review/dt
A IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l20 and review/dt
L21            1 L20 AND REVIEW/DT

=> d l21, ibib abs, 1

L21  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
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Full Text | Cited References

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ACCESSION NUMBER:         2004:405479  HCAPLUS
DOCUMENT NUMBER:          141:46634
TITLE:                    Other antidepressants
AUTHOR(S):                Preskorn, S. H.; Ross, R.
CORPORATE SOURCE:         Department of Psychiatry and Behavioral Sciences,
                          Psychiatric Research Institute, University of Kansas
                          School of Medicine, Wichita, KS, KA 67214, USA
SOURCE:                   Handbook of Experimental Pharmacology (2004),
                          157(Antidepressants), 263-324
                          CODEN: HEPHD2; ISSN: 0171-2004
PUBLISHER:                Springer-Verlag
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review.  This chapter reviews the following antidepressants, which do
     not belong to one of the major classes described in the three preceding
     chapters: bupropion, mirtazapine and mianserin, nefazodone and trazodone,
     reboxetine, venlafaxine, duloxetine, milnacipran, and tianeptine.
     Unlike the selective serotonin reuptake inhibitors (SSRIs), many of these
     antidepressants have an ascending rather than a flat dose-response curve.
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The chapter provides a brief review of the chem., pharmacol., metab., safety and adverse effects, clin. use, and therapeutic indications of each antidepressant. Bupropion is a weak dual uptake inhibitor of both dopamine and norepinephrine (NE). Information concerning its pharmacodynamic and pharmacokinetic properties is limited, primarily because of the age of the drug (clin. trials begun in the mid-1970s). Bupropion's most serious side effect is dose-dependent seizures, so that the highest recommended doses are 450 and 400 mg/day for the immediate release (IR) and sustained release (SR) formulations, resp. Other adverse effects include restlessness, activation, tremors, insomnia, and nausea. Bupropion was found to be an effective antidepressant in several double-blind studies that generally used doses higher than the max. recommended dose of 450 mg/day. Despite fairly modest evidence of antidepressant efficacy, bupropion may be useful in a no. of clin. situations, including for patients with prominent psychomotor retardation, Parkinson's disease, or attention-deficit/hyperactivity disorder; for patients who have failed to respond to other antidepressants; and for patients who cannot tolerate sexual side effects of other antidepressants. Bupropion has also been approved as an aid in smoking cessation. Mirtazapine and its forerunner mianserin, are tetracyclic compds. with a unique mechanism of action. Mirtazapine is an α2-antagonist that increases noradrenergic and serotonergic neurotransmission, the primary mechanism thought to underlie its antidepressant activity. Mirtazapine does not cause many of the side effects assocd. with the SSRIs (e.g., nausea, loose stools, disturbed sleep pathol., sexual dysfunction) and causes minimal anticholinergic effects, no quinidine-like effects, and no effects on blood pressure. Sedation can be a problem, esp. early in treatment, although this may be an advantage for patients with prominent insomnia, anxiety, or agitation. Mirtazapine can cause increased appetite and wt. gain, transient neutropenia, and transient mild elevations of liver function tests. Three cases of agranulocytosis were reported out of 3,000 patients in the mirtazapine clin. trial program, an incidence too low to draw any conclusion about cause and effect. Although postmarketing experience has not found an unusual no. of cases of agranulocytosis, the package insert in the United States contains a warning that a white blood cell count should be done if a patient taking mirtazapine develops signs of fever or infection. Because of its unique mechanism of action, mirtazapine may be efficacious for patients who have not benefited from other types of antidepressants. Nefazodone and trazodone have chem. related structures that incorporate 5-HT2A receptor blockade plus weak 5-HT uptake blockade and possibly NE uptake blockade. Trazodone is widely used as a nonhabit-forming sleep aid rather than as an antidepressant. The antihistaminergic properties of trazodone are partly responsible for its popularity as a sleep aid, but can cause significant problems with daytime sedation when it is used as an antidepressant; however, it may be useful for treating agitation in geriatric patients. Nefazodone, a more potent serotonin re-uptake inhibitor (SRI) than trazodone, was designed with the goal of producing a better antidepressant than trazodone, although it is a much weaker SRI than the SSRIs or **venlafaxine**. Because it substantially inhibits CYP 3A3/4, nefazodone can elevate levels of coprescribed drugs metabolized via CYP 3A/3/4. Nefazodone produces less activation and sexual dysfunction than the SSRIs and **venlafaxine**; it does not cause blood pressure elevation or disturb sleep physiol.; it improves subjective sleep quality. The incidence and severity of the following adverse effects increase in a dose-dependent fashion as a function of the starting dose of nefazodone: dizziness/lightheadedness, confusion, sedation, gastrointestinal side effects. Nefazodone appears to have efficacy in patients with clin. depression and prominent anxiety. Although there appears to be greater interpatient variability in response to nefazodone than to many of the other newer antidepressants, nefazodone

can be a useful option for patients who are unable to tolerate the adverse effects of the SSRIs. Reboxetine is a selective NE reuptake pump inhibitor. Its most common adverse effects are insomnia, sweating, constipation, dry mouth, and urinary hesitancy. Most of the published trials of reboxetine have been active rather than placebo-controlled and results were not published in full with rigorous peer review, compromising the ability to make an assessment of efficacy. Sufficient evidence of the efficacy of reboxetine in major depression has not been presented to receive approval for marketing in the United States, but reboxetine is available in several other countries. **Venlafaxine**, a phenylethylamine, first inhibits the neuronal uptake pump for serotonin (SE) and then at higher concns. inhibits the uptake pump for NE. Unlike tertiary amine tricyclic antidepressants (TCAs), which also inhibit the SE and NE uptake pumps, **venlafaxine** has low affinity for most other neural receptors and does not inhibit sodium fast channels, making it relatively safe in overdose. Its adverse effects change qual. as the dose increases because of progressively greater blockade of NE uptake with increasing doses. At low doses, the adverse-effect profile is similar to an SSRI with nausea, loose stools, sexual dysfunction, while **venlafaxine** at higher doses can produce generally mild increases in blood pressure, diaphoresis, tachycardia, tremors, and anxiety. A disadvantage of **venlafaxine** relative to the SSRIs is the potential for dose-dependent blood pressure elevation, most likely due to the NE uptake inhibition caused by higher doses; however, this adverse effect is infrequently obsd. at doses below 225 mg/day. **Venlafaxine** and the SSRIs have similar advantages over the TCAs and monoamine oxidase inhibitors. **Venlafaxine** also has a no. of potential advantages over the SSRIs, including an ascending dose-antidepressant response curve, with possible greater overall efficacy at higher doses, evidence of more rapid onset of antidepressant action, evidence of superior efficacy in hospitalized patients with major depressive disorder compared with placebo or fluoxetine, and minimal effects on CYP enzymes in contrast to fluoxetine, fluvoxamine, paroxetine, and the non-SSRI, bupropion. Duloxetine is a SE-NE re-uptake pump inhibitor, which is pending approval in the United States and other countries in late 2003. It will be the third member of this pharmacol. class, which also contains **venlafaxine** and milnacipran (sibutramine, the fourth member of this class, is marketed for obesity rather than major depression). Only a limited no. of articles have been published on this compd. but more should be expected shortly after its market introduction. The manufacturer is initially seeking indications for both major depression and **urinary incontinence**. Due to its inhibition of the SE and NE uptake pumps, duloxetine will undoubtedly carry a warning against use in combination with monoamine oxidase inhibitors. It is also a moderate inhibitor of CYP 2D6, so that modest dose redns. and careful monitoring will be needed when prescribing duloxetine in combination with drugs that are preferentially metabolized by CYP 2D6, particularly those with narrow therapeutic indexes. The most common side effects identified in clin. trials to date appear to be nausea, dry mouth, dizziness, constipation, insomnia, asthenia, and hypertension, consistent with its mechanisms of action. Clin. trials to date have demonstrated rates of response and remission in patients with major depression that are comparable to other marketed antidepressants reviewed in this book. Although milnacipran is marketed in France, Japan, and a few other countries, its development in the United States was discontinued. It is an SE and NE reuptake inhibitor in the same class as **venlafaxine**, duloxetine, and the anti-obesity drug, sibutramine. Milnacipran would be predicted to be susceptible to the same pharmacodynamic drug-drug interactions as other drugs in this class, but would not be expected to be involved in any CYP enzyme-mediated drug-drug interactions. Milnacipran at doses of 50-200 mg/day has a favorable adverse-effect profile when

compared with tertiary amine TCAs, including a lower incidence of abnormal liver function tests. At doses of 50 or 100 mg twice a day but not 100 mg once a day, it caused a lower incidence of nausea and anxiety but a higher incidence of headache, dry mouth, and dysuria than did fluoxetine, 20 mg/day, or fluvoxamine, 100 mg twice a day. As with other drugs in this class, dysuria is the most common troublesome and dose-dependent adverse effect (occurring in up to 7% of patients). High-dose milnacipran has been reported to cause blood pressure elevation. Like reboxetine, most of the published trials of milnacipran have been active rather than placebo-controlled and results were not published in full with rigorous peer review, compromising the ability to make an assessment of efficacy; however, findings to date suggest that milnacipran produces a superior antidepressant response compared with placebo at doses of 50 and 100 mg twice a day. Tianeptine is marketed in France but few other countries around the world and there is little knowledge of this drug in the United States and other English-speaking countries. However, a surprising amt. of research, particularly preclin., has been done with tianeptine, in part because of its apparent novel mechanism of action: Tianeptine, in contrast to most other antidepressants, increases SE uptake into neurons rather than blocking it. However, its side-effect profile is similar to that of other newer antidepressants, with low abuse potential and a low risk of adverse effects on the cardiovascular system, the cholinergic systems, sleep/arousal, cognition, psychomotor functioning, and wt. The most common adverse effects include nausea, constipation, abdominal pain, headache, dizziness, and altered dreaming. Hepatotoxicity has been reported but is rare. Like reboxetine and milnacipran, most of the published trials of tianeptine have been active rather than placebo-controlled and results were not published in full with rigorous peer review, compromising the ability to assess efficacy; however, trials to date do suggest efficacy in patients with major depression.

REFERENCE COUNT: 279 THERE ARE 279 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s central () nervous () system? () disorder?
L22       3134 CENTRAL (W) NERVOUS (W) SYSTEM? (W) DISORDER?

=> s l22 and urinary () incontinence?
L23         18 L22 AND URINARY (W) INCONTINENCE?

=> s l23 and review/dt
L24          1 L23 AND REVIEW/DT

=> d l24, ibib abs, 1

L24  ANSWER 1 OF 1     MEDLINE on STN
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Full Text | Citing References

ACCESSION NUMBER: 77039644 MEDLINE
DOCUMENT NUMBER: PubMed ID: 790743
TITLE: Nomenclature of neurogenic bladder.
AUTHOR: Gibbon N O
SOURCE: Urology, (1976 Nov) 8 (5) 423-31. Ref: 29
Journal code: 0366151. ISSN: 0090-4295.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 197612
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19990129
Entered Medline: 19761223

AB Vesicourethral physiology is reviewed briefly in the light of recent developments. The effect on bladder function of **central nervous system disorders** is considered and attention is drawn to the desirability of diverting interest from the bladder to the urethra in neuropathic cases. It is concluded that there are only two basic types of neuropathic bladder function--in lesions of and above the sacral reflex pathways, respectively. Neurologically these are classified according to the condition of the anal and bulbocavernosus reflexes and the ice water test.

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=> s chronic () obstructive () pulmonary () disease?
L25      37137 CHRONIC (W) OBSTRUCTIVE (W) PULMONARY (W) DISEASE?

=> d his

     (FILE 'HOME' ENTERED AT 12:05:34 ON 22 NOV 2005)

     FILE 'REGISTRY' ENTERED AT 12:09:17 ON 22 NOV 2005

     FILE 'MEDLINE, BIOSIS, EMBASE, HCAPLUS' ENTERED AT 12:09:40 ON 22 NOV 2005
L1            0 S VENLAFAXINE () POST () TRAUMATIC () STRESS
L2            7 S VENLAFAXINE? () DERIVATIVE?
L3            1 S VENLAFAXINE () ANALOG?
L4            0 S L2 AND REVIEW/DT
L5         8967 S VENLAFAXINE?
L6       626478 S SENILE () DEMENTIA? OR PARKINSON? () DISEASE? OR EPILEPSY? OR
L7           12 S L6 ()  L5
L8            1 S L7 AND REVIEW/DT
L9       187794 S SCHIZOPHRENIA OR BORDERLINE () PERSONALITY () DISORDER?
L10           1 S L9 () L5
L11           0 S L10 AND REVIEW/DT
L12        4026 S COCAINE () ADDICTION OR ALCOHOL () ADDICTION?
L13           0 S L12 () L5
L14           9 S L12 AND L5
L15           0 S L14 AND REVIEW/DT
L16       16028 S BULIMIA () NERVOSA? OR GILLES? () TOURETTE () SYNDROME OR VAS
L17           0 S L16 () L5
L18          66 S L16 AND L5
L19           4 S L18 AND REVIEW/DT
L20          36 S L5 AND URINARY () INCONTINENCE?
L21           1 S L20 AND REVIEW/DT
L22        3134 S CENTRAL () NERVOUS () SYSTEM? () DISORDER?
L23          18 S L22 AND URINARY () INCONTINENCE?
L24           1 S L23 AND REVIEW/DT
L25       37137 S CHRONIC () OBSTRUCTIVE () PULMONARY () DISEASE?

=> s l25 and l5
L26           1 L25 AND L5

=> s l26 and review/dt
L27           0 L26 AND REVIEW/DT

=> s l5 and pain?
L28         780 L5 AND PAIN?
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=> s l5 () pain
L29           3 L5 (W) PAIN

=> s l29 and review/dt
L30           1 L29 AND REVIEW/DT

=> d l30, ibib abs, 1

L30  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
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Full Text | More References

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ACCESSION NUMBER:         2002:580046  HCAPLUS
DOCUMENT NUMBER:          137:149663
TITLE:                    Antidepressants in pain management
AUTHOR(S):                Carter, Gregory T.; Sullivan, Mark D.
CORPORATE SOURCE:         Department of Rehabilitation Medicine, University of
                          Washington School of Medicine, Seattle, WA, 98195, USA
SOURCE:                   Current Opinion in Investigational Drugs (PharmaPress
                          Ltd.) (2002), 3(3), 454-458
                          CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER:                PharmaPress Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB    A review.  Antidepressants exhibit a no. of pharmacol. mechanisms,
      including norepinephrine and serotonin modulation, direct and indirect
      effects on opioid receptors, inhibition of histamine, cholinergic and
      N-methyl-D-aspartate receptors, and inhibition of ion channel activity.
      Although it is not entirely clear which mechanisms produce analgesia and
      to what extent, the available animal and clin. trials data indicates that
      tricyclic antidepressants are effective in treating many types of pain.
      The newer selective serotonin reuptake inhibitors also appear to be
      effective for chronic headache and other non-neuropathic forms of chronic
      pain but are not as well studied.  This article reviews the current basic
      and clin. research on antidepressants in pain management.
REFERENCE COUNT:          59    THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


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     (FILE 'HOME' ENTERED AT 12:05:34 ON 22 NOV 2005)

     FILE 'REGISTRY' ENTERED AT 12:09:17 ON 22 NOV 2005

     FILE 'MEDLINE, BIOSIS, EMBASE, HCAPLUS' ENTERED AT 12:09:40 ON 22 NOV 2005
L1            0 S VENLAFAXINE () POST () TRAUMATIC () STRESS
L2            7 S VENLAFAXINE? () DERIVATIVE?
L3            1 S VENLAFAXINE () ANALOG?
L4            0 S L2 AND REVIEW/DT
L5         8967 S VENLAFAXINE?
L6       626478 S SENILE () DEMENTIA? OR PARKINSON? () DISEASE? OR EPILEPSY? OR
L7           12 S L6 ()  L5
L8            1 S L7 AND REVIEW/DT
L9       187794 S SCHIZOPHRENIA OR BORDERLINE () PERSONALITY () DISORDER?
L10           1 S L9 () L5
L11           0 S L10 AND REVIEW/DT
L12        4026 S COCAINE () ADDICTION OR ALCOHOL () ADDICTION?
L13           0 S L12 () L5
L14           9 S L12 AND L5
L15           0 S L14 AND REVIEW/DT
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and fibromyalgia, can be challenging for primary care providers to treat. Antidepressants that block reuptake of both serotonin and norepinephrine, such as the tricyclic antidepressants (e.g., amitriptyline), have been used to treat pain syndromes in patients with or without comorbid MDD or GAD. **Venlafaxine**, a serotonin and norepinephrine reuptake inhibitor, has been safe and effective in animal models, healthy human volunteers, and patients for treatment of various pain syndromes. The use of **venlafaxine** for treatment of pain associated with MDD or GAD, neuropathic pain, headache, fibromyalgia, and postmastectomy pain syndrome is reviewed. Currently, no antidepressants, including **venlafaxine**, are approved for the treatment of chronic pain syndromes. Additional randomized, controlled trials are necessary to fully elucidate the role of **venlafaxine** in the treatment of chronic pain.

L34 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:583658 HCAPLUS
DOCUMENT NUMBER: 141:184422
TITLE: Treatment of pain syndromes with **venlafaxine**
AUTHOR(S): Grothe, Dale R.; Scheckner, Brian; Albano, Dominick
CORPORATE SOURCE: Global Medical Communications, Neuroscience, Wyeth Pharmaceuticals, Collegeville, PA, USA
SOURCE: Pharmacotherapy (2004), 24(5), 621-629
CODEN: PHPYDQ; ISSN: 0277-0008
PUBLISHER: Pharmacotherapy Publications
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Major depressive disorder (MDD) and anxiety disorders such as generalized anxiety disorder (GAD) are often accompanied by chronic painful symptoms. Examples of such symptoms are backache, headache, gastrointestinal pain, and joint pain. In addn., pain generally not assocd. with major depression or an anxiety disorder, such as peripheral neuropathic pain (e.g., diabetic neuropathy and **postherpetic neuralgia**), cancer pain, and fibromyalgia, can be challenging for primary care providers to treat. Antidepressants that block reuptake of both serotonin and norepinephrine, such as the tricyclic antidepressants (e.g., amitriptyline), have been used to treat pain syndromes in patients with or without comorbid MDD or GAD. **Venlafaxine**, a serotonin and norepinephrine reuptake inhibitor, has been safe and effective in animal models, healthy human volunteers, and patients for treatment of various pain syndromes. The use of **venlafaxine** for treatment of pain assocd. with MDD or GAD, neuropathic pain, headache, fibromyalgia, and postmastectomy pain syndrome is reviewed. Currently, no antidepressants, including **venlafaxine**, are approved for the treatment of chronic pain syndromes. Addnl. randomized, controlled trials are necessary to fully elucidate the role of **venlafaxine** in the treatment of chronic pain.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:469364 HCAPLUS
DOCUMENT NUMBER: 129:239318
TITLE: Potential applications of **venlafaxine**
AUTHOR(S): Nutt, D.; Johnson, F. Neil
CORPORATE SOURCE: School of Medical Sciences, University of Bristol, Bristol, BS8 1TD, UK
SOURCE: Reviews in Contemporary Pharmacotherapy (1998), 9(5),

321-331
CODEN: RCPHFW; ISSN: 0954-8602
PUBLISHER: Marius Press
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 95 refs. The action of **venlafaxine** on at least two neurotransmitter systems suggests that this agent may have potential applications in a variety of conditions in addn. to the treatment of depression. Evidence on the point is relatively scanty at the present time, but such information as is available suggests that **venlafaxine** may have a future role in the management of several psychiatric conditions. These include: obsessive-compulsive disorder; panic disorder; attention deficit hyper-activity disorder (in children and in adults); borderline personality disorder; chronic fatigue syndrome; and possibly loss of libido and/or erectile dysfunction. There are also suggestions of therapeutic benefit arising from **venlafaxine** treatment of phobic conditions, specifically agoraphobia and social phobia. Recent work indicates that **venlafaxine** may reduce anxiety concomitant with depressive symptoms as well as anxiety occurring in the absence of depression, and that it may be rather more effective in doing so than is the case for several comparator agents. **Venlafaxine** appears to be effective in treating certain forms of pain; this is particularly evident against some types of headache, and there are indications of efficacy also against **postherpetic neuralgia**, chronic radicular back pain, and fibromyalgia. While **venlafaxine** has been found to show some degree of efficacy against Raynaud's phenomenon, it is unlikely to be better than selective serotonin reuptake inhibitors in the treatment of this condition. Further studies of **venlafaxine** are likely to reveal a wider spectrum of potential applications for this agent.

REFERENCE COUNT: 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 12:05:34 ON 22 NOV 2005)

FILE 'REGISTRY' ENTERED AT 12:09:17 ON 22 NOV 2005

FILE 'MEDLINE, BIOSIS, EMBASE, HCAPLUS' ENTERED AT 12:09:40 ON 22 NOV 2005

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L1            0 S VENLAFAXINE () POST () TRAUMATIC () STRESS
L2            7 S VENLAFAXINE? () DERIVATIVE?
L3            1 S VENLAFAXINE () ANALOG?
L4            0 S L2 AND REVIEW/DT
L5         8967 S VENLAFAXINE?
L6       626478 S SENILE () DEMENTIA? OR PARKINSON? () DISEASE? OR EPILEPSY? OR
L7           12 S L6 ()  L5
L8            1 S L7 AND REVIEW/DT
L9       187794 S SCHIZOPHRENIA OR BORDERLINE () PERSONALITY () DISORDER?
L10           1 S L9 () L5
L11           0 S L10 AND REVIEW/DT
L12        4026 S COCAINE () ADDICTION OR ALCOHOL () ADDICTION?
L13           0 S L12 () L5
L14           9 S L12 AND L5
L15           0 S L14 AND REVIEW/DT
L16       16028 S BULIMIA () NERVOSA? OR GILLES? () TOURETTE () SYNDROME OR VAS
L17           0 S L16 () L5
L18          66 S L16 AND L5
L19           4 S L18 AND REVIEW/DT
L20          36 S L5 AND URINARY () INCONTINENCE?
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L21           1 S L20 AND REVIEW/DT
L22        3134 S CENTRAL () NERVOUS () SYSTEM? () DISORDER?
L23          18 S L22 AND URINARY () INCONTINENCE?
L24           1 S L23 AND REVIEW/DT
L25       37137 S CHRONIC () OBSTRUCTIVE () PULMONARY () DISEASE?
L26           1 S L25 AND L5
L27           0 S L26 AND REVIEW/DT
L28         780 S L5 AND PAIN?
L29           3 S L5 () PAIN
L30           1 S L29 AND REVIEW/DT
L31        3164 S POSTHERPETIC () NEURALGIA?
L32           0 S L31 () L5
L33          43 S L31 AND L5
L34           4 S L33 AND REVIEW/DT

=> s sexual () dysfunction and l5
L35         633 SEXUAL (W) DYSFUNCTION AND L5

=> s l35 and review/dt
L36          23 L35 AND REVIEW/DT

=> s sexual () dysfunction?
L37       17772 SEXUAL (W) DYSFUNCTION?

=> s l5 () l37
L38           1 L5 (W) L37

=> s l38 and review/dt
L39           0 L38 AND REVIEW/DT

=> d l36, ibib abs, 1-4

L36  ANSWER 1 OF 23     MEDLINE on STN
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Full Text | Citing References

ACCESSION NUMBER: 2004248907 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15147109
TITLE: Tolerability issues during long-term treatment with antidepressants.
AUTHOR: Cassano Paolo; Fava Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Boston, Massachusetts 02114, USA.. Pcassano@partners.org
SOURCE: Annals of clinical psychiatry : official journal of the American Academy of Clinical Psychiatrists, (2004 Jan-Mar) 16 (1) 15-25. Ref: 111
Journal code: 8911021. ISSN: 1040-1237.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040520
Last Updated on STN: 20040811
Entered Medline: 20040810

AB Depressive disorders are highly prevalent in the general population. Long-term treatment with antidepressants consolidates the improvement obtained during the acute phase of the treatment and prevents relapses and recurrences of the disorder. On the other hand, there is growing evidence

that antidepressant side effects may limit patients' quality of life and social functioning, as well as affect patients' health and treatment adherence. Most studies concerning antidepressant treatment have focused on short-term tolerability, ignoring both early-onset persistent side effects and late-onset side effects that are reported during long-term treatment. Nevertheless, these long-term treatment side effects are likely to have a dramatic impact on patient outcome and treatment adherence. Common long-term side effects of antidepressants are weight gain, **sexual dysfunction**, sleep disturbances, fatigue, apathy, and cognitive impairment (e.g., working memory dysfunction). Usual strategies for the management of these long-term side effects are: changing drug daily schedule, various augmentation therapies, antidepressant switches, drug-holidays, and dose tapering, with the latter two strategies being strongly discouraged on the basis of concerns that patients' depressive episodes may return. Selective serotonin reuptake inhibitors (SSRIs) and atypical antidepressants (e.g., **venlafaxine**, bupropion, and nefazodone) show a relatively favorable short-term as well as long-term tolerability compared with older drugs (e.g., tricyclics and monoamine oxidase inhibitors). Therefore, clinicians are likely to prefer them in usual practice, especially among patients requiring maintenance treatment. The present review focuses on management of long-term side effects.

L36 ANSWER 2 OF 23 MEDLINE on STN

Full Text | Citing References

ACCESSION NUMBER: 2004050011 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14750401
TITLE: Diabetic neuropathy: an intensive review.
COMMENT: Comment in: Am J Health Syst Pharm. 2004 Jul 15;61(14):1446-7; author reply 1447. PubMed ID: 15332691
AUTHOR: Duby Jeremiah John; Campbell R Keith; Setter Stephen M; White John Raymond; Rasmussen Kristin A
CORPORATE SOURCE: University of Arizona, Tucson, AZ, USA.
SOURCE: American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists, (2004 Jan 15) 61 (2) 160-73; quiz 175-6. Ref: 90
Journal code: 9503023. ISSN: 1079-2082.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20040131
Last Updated on STN: 20040414
Entered Medline: 20040413

AB PURPOSE: The epidemiology, classification, pathology, and treatment of diabetic neuropathy are reviewed. SUMMARY: Diabetic peripheral neuropathy is a common complication of diabetes that can cause significant morbidity and mortality. Some 30% of hospitalized and 20% of community-dwelling diabetes patients have peripheral neuropathy; the annual incidence rate is approximately 2%. The primary risk factor is hyperglycemia. Sensorimotor neuropathy is marked by pain, paresthesia, and sensory loss. Cardiac autonomic neuropathy (CAN) may contribute to myocardial infarction, malignant arrhythmia, and sudden death. Gastroparesis is the most debilitating complication of gastrointestinal autonomic neuropathy. Genitourinary autonomic neuropathy can cause **sexual dysfunction** and neurogenic bladder. The pathology of diabetic neuropathy involves oxidative stress, advanced glycation end products, polyol pathway flux,

and protein kinase C activation; all contribute to microvascular disease and nerve dysfunction. For symptom management current evidence from clinical trials supports the use of desipramine, amitriptyline, capsaicin, tramadol, gabapentin, bupropion, and **venlafaxine** as preferred medications. Citalopram, nonsteroidal antiinflammatory drugs, and opioid analgesics may be used as adjuvant agents. Lamotrigine, oxcarbazepine, paroxetine, levodopa, and alpha-lipoic acid are alternative considerations. Evidence supporting the use of zonisamide, fluoxetine, mexiletine, dextromethorphan, and phenytoin is considered equivocal. Complementary therapies have also shown efficacy. The symptoms of CAN may be ameliorated with fludrocortisone, clonidine, midodrine, dihydroergotamine or caffeine, octreotide, and beta-blockers. Gastroparesis may be treated with metoclopramide or erythromycin. The most promising disease-modifying therapy is ruboxistaurin, which is in Phase III trials. Glycemic control remains the foundation of prevention and the prerequisite of adequate treatment. CONCLUSION: Diabetic neuropathy is a many-faceted complication of diabetes that can be managed symptomatically with an array of drugs.

L36 ANSWER 3 OF 23 MEDLINE on STN

Full Text | More References

ACCESSION NUMBER: 2003152679 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12667885
TITLE: Side effects of androgen deprivation therapy: monitoring and minimizing toxicity.
AUTHOR: Higano Celestia S
CORPORATE SOURCE: Department of Urology, University of Washington School of Medicine, University of Washington, Seattle Cancer Care Alliance, Seattle, Washington 98109, USA..
thigano@uwashington.edu
SOURCE: Urology, (2003 Feb) 61 (2 Suppl 1) 32-8. Ref: 43
Journal code: 0366151. ISSN: 1527-9995.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030402
Last Updated on STN: 20030702
Entered Medline: 20030701

AB The current trends in favor of androgen deprivation therapy (ADT) for nonmetastatic prostate cancer at the stage of biochemical recurrence or increasing prostate-specific antigen (PSA) raises the issue of exposing otherwise asymptomatic patients to potential side effects over the longer term. Some of these side effects can have deleterious effects on quality of life, and others may contribute to increased risks for serious health concerns associated with aging. Sexual side effects are the most well-recognized adverse effects from ADT and include loss of libido, erectile dysfunction (ED), and hot flashes. Loss of libido is distressing to many men, and they may not pursue treatments for ED. However, for those who do maintain sexual interest, various remedies are available. The incidence of hot flashes, which may not abate over the course of ADT, is close to 80%. Estrogens, progestin megestrol acetate, medroxyprogesterone acetate, **venlafaxine**, and cyproterone acetate have been shown to alleviate hot flashes and associated symptoms. Physiologic effects, including gynecomastia, changes in body composition (weight gain, reduced muscle mass, increase in body fat), and changes in lipids, are

less commonly recognized as side effects of ADT. These may lead to an exacerbation of potentially more serious conditions, such as hypertension, diabetes, and coronary artery disease. Loss of bone mineral density, anemia, and hair changes also may occur. Additionally, both the diagnosis of prostate cancer and the hormonal therapy can cause psychological distress. These side effects need more systematic study in clinical trials. Physicians should be aware of far-reaching consequences of ADT and should incorporate strategies for preventing and managing toxicities into routine practice.

L36 ANSWER 4 OF 23 MEDLINE on STN

Full Text | Citing References

ACCESSION NUMBER: 2003076790 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12588077
TITLE: Antidepressants: update on new agents and indications.
COMMENT: Comment in: Am Fam Physician. 2004 Jun 1;69(11):2528; author reply 2528. PubMed ID: 15202688
Erratum in: Am Fam Physician. 2003 May 1;67(9):1874
Erratum in: Am Fam Physician. 2004 Mar 1;69(5):1049
AUTHOR: Ables Adrienne Z; Baughman Otis L 3rd
CORPORATE SOURCE: Spartanburg Family Medicine Residency Program, Spartanburg, South Carolina 29303, USA.. aables@srhs.com
SOURCE: American family physician, (2003 Feb 1) 67 (3) 547-54.
Ref: 45
Journal code: 1272646. ISSN: 0002-838X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030218
Last Updated on STN: 20030313
Entered Medline: 20030312

AB A number of antidepressants have emerged in the U.S. market in the past two decades. Selective serotonin reuptake inhibitors have become the drugs of choice in the treatment of depression, and they are also effective in the treatment of obsessive-compulsive disorder, panic disorder, and social phobia. New indications for selective serotonin reuptake inhibitors include post-traumatic stress disorder, premenstrual dysphoric disorder, and generalized anxiety disorder. Extended-release **venlafaxine** has recently been approved by the U.S. Food and Drug Administration for the treatment of generalized anxiety disorder. Mirtazapine, which is unrelated to the selective serotonin reuptake inhibitors, is unique in its action--stimulating the release of norepinephrine and serotonin. The choice of antidepressant drug depends on the agent's pharmacologic profile, secondary actions, and tolerability. **Sexual dysfunction** related to the use of antidepressants may be addressed by reducing the dosage, switching to another agent, or adding another drug to overcome the sexual side effects. Augmentation with lithium or triiodothyronine may be useful in patients who are partially or totally resistant to antidepressant treatment. Finally, tapering antidepressant medication may help to avoid discontinuation syndrome or antidepressant withdrawal.

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L40 2 L5 (W) COGNITION?

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L41             0 L40 AND REVIEW/DT

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NEWS EXPRESS NOVEMBER 18 CURRENT VERSION FOR WINDOWS IS V8.01,
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=> s venlafaxine () derivative?
L1            7 VENLAFAXINE (W) DERIVATIVE?

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L1   ANSWER 3 OF 7  HCAPLUS  COPYRIGHT 2005 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:         2004:740168  HCAPLUS
DOCUMENT NUMBER:          141:265967
TITLE:                    Silicon derivatives of venlafaxine for the treatment
                          or prevention of psoriasis or panic disorder
INVENTOR(S):              Showell, Graham Andrew
PATENT ASSIGNEE(S):       Amedis Pharmaceuticals Ltd., UK
SOURCE:                   PCT Int. Appl., 15 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2004075902         A1    20040910    WO 2004-GB662            20040219
         W:  AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,
             BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
             CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
             ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
             IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,
             LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,
             MZ, MZ, NA, NI
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
             BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
             MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                          GB 2003-4646        A  20030228
                                                GB 2003-4647        A  20030228
OTHER SOURCE(S):          MARPAT 141:265967
AB   A silicon deriv. of venlafaxine such as 1-[2-dimethylamino-1-(4-
     methoxyphenyl)ethyl]-1-silacyclohexan-1-ol or a salt thereof or a prodrug
     form that is hydrolyzable for the manuf. of a medicament for the treatment
     or prevention of psoriasis or panic disorder is disclosed.
REFERENCE COUNT:          5     THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1   ANSWER 4 OF 7  HCAPLUS  COPYRIGHT 2005 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:         2000:725583  HCAPLUS
DOCUMENT NUMBER:          133:296268
TITLE:                    Preparation of derivatives of venlafaxine and their
                          inhibition of neuronal monoamine reuptake
INVENTOR(S):              Jerussi, Thomas P.; Senanayake, Chrisantha H.
PATENT ASSIGNEE(S):       Sepracor Inc., USA
SOURCE:                   PCT Int. Appl., 40 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059851	A1	20001012	WO 2000-US8705	20000331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2368083	AA	20001012	CA 2000-2368083	20000331
EP 1165487	A1	20020102	EP 2000-920026	20000331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003521470	T2	20030715	JP 2000-609367	20000331
NZ 514612	A	20040130	NZ 2000-514612	20000331
EP 1466889	A1	20041013	EP 2004-10248	20000331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
AU 782092	B2	20050630	AU 2000-40627	20000331
NO 2001004816	A	20011204	NO 2001-4816	20011003
US 2004106576	A1	20040603	US 2003-720134	20031125
US 2005197392	A1	20050908	US 2005-91518	20050329

PRIORITY APPLN. INFO.:	US 1999-127938P	P	19990406
	US 1999-167906P	P	19991130
	US 2000-527442	A3	20000317
	EP 2000-920026	A3	20000331
	WO 2000-US8705	W	20000331
	US 2003-720134	A3	20031125

AB Prepn. of derivs. of venlafaxine, e.g., O-desmethylvenlaflaxine, is described. Also disclosed are methods of treating and preventing diseases and disorders including, but not limited to, affective disorders such as depression, bipolar and manic disorders, attention deficit disorder, attention deficit disorder with hyperactivity, Parkinson's disease, epilepsy, cerebral function disorders, obesity and wt. gain, incontinence, dementia and related disorders.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:384124 HCAPLUS
DOCUMENT NUMBER: 133:17270
TITLE: Preparation of (-)-venlafaxine and derivatives as neuronal monoamine reuptake inhibitors.
INVENTOR(S): Jerussi, Thomas P.; Senanayake, Chrisantha H.
PATENT ASSIGNEE(S): Sepracor Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032556	A1	20000608	WO 1999-US28303	19991201
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6342533	B1	20020129	US 1999-450690	19991130
CA 2352324	AA	20000608	CA 1999-2352324	19991201
EP 1135359	A1	20010926	EP 1999-968056	19991201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003524613	T2	20030819	JP 2000-585198	19991201
AU 774408	B2	20040624	AU 2000-24749	19991201
US 2002086904	A1	20020704	US 2001-14592	20011214
US 6441048	B2	20020827		
US 2003018083	A1	20030123	US 2002-222815	20020819
US 6911479	B2	20050628		
US 2004180952	A1	20040916	US 2004-806423	20040323

PRIORITY APPLN. INFO.:

US 1998-110488P	P	19981201
US 1999-450690	A	19991130
WO 1999-US28303	W	19991201
US 2001-14592	A3	20011214
US 2002-222815	A3	20020819

AB A pharmaceutical compn. comprising (-)-**venlafaxine deriv.** substantially free of (+)-stereoisomer is claimed. Thus, (?)-venlafaxine in THF was added to a mixt. prepd. from Ph2PH and BuLi in THF at 0? followed by stirring and overnight reflux to give 73.8% (?)-O-desmethylvenlafaxine, which was resolved using di-p-toluoyl-L-tartaric acid to give (-)-O-desmethylvenlafaxine. Drug formulations contg. the latter are given.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Cited References

ACCESSION NUMBER: 2000:384122 HCAPLUS
DOCUMENT NUMBER: 133:30575
TITLE: Preparation of derivatives of (+)-venlafaxine as inhibitors of neuronal monoamine reuptake.
INVENTOR(S): Jerussi, Thomas P.; Senannayake, Chrisantha H.
PATENT ASSIGNEE(S): Sepracor Inc., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032555	A1	20000608	WO 1999-US28306	19991201
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,				

MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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US 6197828	B1	20010306	US 1999-450691		19991130
CA 2352321	AA	20000608	CA 1999-2352321		19991201
EP 1135358	A1	20010926	EP 1999-965065		19991201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2003501344	T2	20030114	JP 2000-585197		19991201
PRIORITY APPLN. INFO.:			US 1998-110486P	P	19981201
			US 1999-450691	A	19991130
			WO 1999-US28306	W	19991201

AB A method of treating an affective disorder comprises administration of a (+)-**venlafaxine deriv.** substantially free of the (-)-enantiomer. Thus, (?)-venlafaxine (prepn. given) was added to a 0? mixt. of Ph2PH and BuLi followed by stirring and reflux overnight to give 73.8% (?)-O-desmethylvenlafaxine, which was resolved to give (+)-O-desmethylvenlafaxine. Drug formulations contg. the latter are given.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Cited References

ACCESSION NUMBER: 1998:323132 HCAPLUS
DOCUMENT NUMBER: 129:23447
TITLE: A method for treating tension-type headache
INVENTOR(S): Olesen, Jes; Bendtsen, Lars; Jensen, Rigmor; Madsen, Ulf
PATENT ASSIGNEE(S): Den.
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9819674	A2	19980514	WO 1997-DK502	19971104
WO 9819674	A3	19980716		
W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, ES, FI, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2270531	AA	19980514	CA 1997-2270531	19971104
AU 9748632	A1	19980529	AU 1997-48632	19971104
AU 734490	B2	20010614		
EP 1011656	A2	20000628	EP 1997-911150	19971104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

EP 1132082	A1	20010912	EP 2000-204625	19971104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6284794	B1	20010904	US 1999-304115	19990504
AU 771266	B2	20040318	AU 2001-57775	20010802
US 2002072543	A1	20020613	US 2001-941855	20010830
US 6649605	B2	20031118		
US 2004097562	A1	20040520	US 2003-702497	20031107

PRIORITY APPLN. INFO.:	DK 1996-1243	A 19961105
	US 1996-30294P	P 19961105
	AU 1997-48632	A3 19971104
	EP 1997-911150	A3 19971104
	WO 1997-DK502	W 19971104
	US 1998-85413P	P 19980514
	US 1999-304115	A3 19990504
	US 2001-941855	A3 20010830

AB Tension-type headache is treated by interacting with neuronal transmission in relation to pain in connection with headache in a way which prevents or decreases sensitization of second order nociceptive neurons. In particular, treatment is performed by administration of an effective amt. of a substance which prevents or decreases central sensitization. Important examples of such substances are substances which interact with glutamate neurotransmission, such as glutamate receptor antagonists. Other examples are e.g. substances which interact with nitric oxide, such as nitric oxide synthase (NOS) inhibitors. According to a broader aspect of the invention, tension-type headache is treated by administration of substances which are effective in preventing or decreasing pain in connection with tension-type headache. An addnl. aspect of the invention relates to treatment of tension-type headache by administration of substances which substantially inhibit the activity of NOS. Evidence for central sensitization in chronic myofascial pain, as well as mechanisms of spontaneous tension-type headaches, are also described. Gabapentin and dextromethorphan had a prophylactic effect on chronic tension-type headaches.

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L10 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Cited References

ACCESSION NUMBER: 2004:583658 HCAPLUS
DOCUMENT NUMBER: 141:184422
TITLE: Treatment of pain syndromes with **venlafaxine**
AUTHOR(S): Grothe, Dale R.; Scheckner, Brian; Albano, Dominick
CORPORATE SOURCE: Global Medical Communications, Neuroscience, Wyeth Pharmaceuticals, Collegeville, PA, USA
SOURCE: Pharmacotherapy (2004), 24(5), 621-629
CODEN: PHPYDQ; ISSN: 0277-0008
PUBLISHER: Pharmacotherapy Publications
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Major depressive disorder (MDD) and anxiety disorders such as generalized anxiety disorder (GAD) are often accompanied by **chronic painful** symptoms. Examples of such symptoms are backache, headache, gastrointestinal pain, and joint pain. In addn., pain generally not assocd. with major depression or an anxiety disorder, such as peripheral neuropathic pain (e.g., diabetic neuropathy and postherpetic neuralgia), cancer pain, and fibromyalgia, can be challenging for primary care providers to treat. Antidepressants that block reuptake of both serotonin and norepinephrine, such as the tricyclic antidepressants (e.g., amitriptyline), have been used to treat pain syndromes in patients with or without comorbid MDD or GAD. **Venlafaxine**, a serotonin and norepinephrine reuptake inhibitor, has been safe and effective in animal models, healthy human volunteers, and patients for treatment of various pain syndromes. The use of **venlafaxine** for treatment of pain assocd. with MDD or GAD, neuropathic pain, headache, fibromyalgia, and postmastectomy pain syndrome is reviewed. Currently, no antidepressants, including **venlafaxine**, are approved for the treatment of **chronic pain** syndromes. Addnl. randomized, controlled trials are necessary to fully elucidate the role of **venlafaxine** in the treatment of **chronic pain**.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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NEWS 10	OCT 27	EPFULL enhanced with additional content
NEWS 11	NOV 14	CA/CAplus - Expanded coverage of German academic research

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CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 NOV 2005 HIGHEST RN 868586-21-4
DICTIONARY FILE UPDATES: 21 NOV 2005 HIGHEST RN 868586-21-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************
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Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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=>
Uploading structure

L1      STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 16:52:13 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       19 TO ITERATE

100.0% PROCESSED       19 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          119 TO      641
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 160.90 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:52:17 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      315 TO ITERATE

100.0% PROCESSED      315 ITERATIONS                               15 ANSWERS
SEARCH TIME: 00.00.01

L3           15 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             162.62     162.83

FILE 'HCAPLUS' ENTERED AT 16:52:20 ON 22 NOV 2005
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FILE COVERS 1907 - 22 Nov 2005 VOL 143 ISS 22
FILE LAST UPDATED: 21 Nov 2005 (20051121/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s l3/thu
           109 L3
        731132 THU/RL
L4          38 L3/THU
                (L3 (L) THU/RL)

=> d l4, ibib abs hitstr, 1-38
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L4 ANSWER 1 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | More References

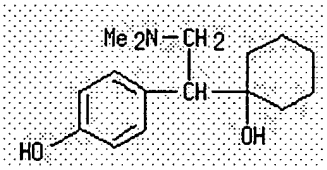
ACCESSION NUMBER: 2005:1175135 HCAPLUS
TITLE: Modified-release compositions of at least one form of venlafaxine
INVENTOR(S): Seth, Pawan; Maes, Paul J.
PATENT ASSIGNEE(S): Biovail Laboratories, Inc., Barbados
SOURCE: U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 244,059.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005244498	A1	20051103	US 2004-3028	20041203
US 2003059466	A1	20030327	US 2001-953101	20010914
US 2003091634	A1	20030515	US 2002-244059	20020913
PRIORITY APPLN. INFO.:			US 2001-953101	A2 20010914
			US 2002-244059	A2 20020913

AB The present invention relates to a modified release compn. of at least one form of venlafaxine, which is an enhanced absorption delayed controlled-release compn. for oral administration suitable for once daily dosing. The compn. comprises a core comprising at least one form of venlafaxine selected from the group consisting of venlafaxine, an active metabolite of venlafaxine, a pharmaceutically acceptable salt of

venlafaxine, a pharmaceutically acceptable salt of an active metabolite of venlafaxine, and combinations thereof, and a pharmaceutically acceptable excipient. The compn. further comprises a modified release coating which substantially surrounds the core. The compns. of the invention provide enhanced absorption delayed controlled release of the at least one form of venlafaxine such that the combined geometric mean ratio of the compn. of the invention to the ref. product for the AUC0-t or the Cmax for venlafaxine and its active metabolite O-desmethylvenlafaxine is greater than 2 after first administration of the compn. under fed or fasting conditions. Tablets contg. venlafaxine hydrochloride 169.71, lactose 71.29, hydroxypropyl Me cellulose 40.00, polyvinylpyrrolidone 2.00 mg in the core and ethocel-100 12.650, Kollidon 90F 7.245, and stearic acid 31.05 mg in the coating were prepd. The amt. of venlafaxine released after 8 h was 100%.

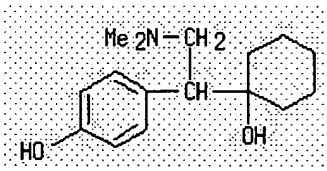
IT **93413-62-8**, O-Desmethylvenlafaxine
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(modified-release compns. of at least one form of venlafaxine)
RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



IT **448904-47-0**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(modified-release compns. of at least one form of venlafaxine)
RN 448904-47-0 HCAPLUS
CN Butanedioic acid, compd. with 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol (1:1) (9CI) (CA INDEX NAME)

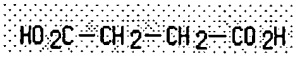
CM 1

CRN 93413-62-8
CMF C16 H25 N O2



CM 2

CRN 110-15-6
CMF C4 H6 O4



L4 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | More References

ACCESSION NUMBER: 2005:1004355 HCAPLUS
DOCUMENT NUMBER: 143:279430
TITLE: Use of D4 and 5-HT2a antagonists, inverse agonists or partial agonists
INVENTOR(S): Buntinx, Erik
PATENT ASSIGNEE(S): Belg.
SOURCE: U.S. Pat. Appl. Publ., 126 pp., Cont.-in-part of U.S. Ser. No. 803,793.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

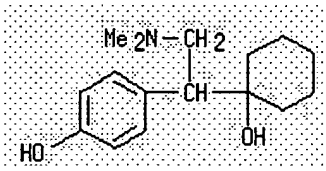
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005203130	A1	20050915	US 2004-984683	20041109
US 2005119253	A1	20050602	US 2003-725965	20031202
US 2005119248	A1	20050602	US 2004-752423	20040106
US 2005119249	A1	20050602	US 2004-803793	20040318
EP 1541197	A1	20050615	EP 2004-25035	20041021
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
WO 2005053796	A1	20050616	WO 2004-BE172	20041202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

US 2003-725965	A2	20031202
EP 2004-447001	A	20040105
US 2004-752423	A2	20040106
US 2004-803793	A2	20040318
EP 2004-25035	A	20041021
CA 2003-2451798	A	20031202
EP 2003-447279	A	20031202
CA 2004-2461248	A	20040318
EP 2004-447066	A	20040318
JP 2004-349085	A	20041104
US 2004-984683	A	20041109
CA 2004-2487529	A	20041115

AB The present invention relates to the use of compds. and compns. of compds. having D4 and 5-HT2A antagonistic, partial agonistic or inverse agonistic activity for the treatment of the underlying dysregulation of the emotional functionality of mental disorders (i.e. affect instability-hypersensitivity-hyperesthesia-dissociative phenomena-etc.). The invention also relates to methods comprising administering to a patient diagnosed as having a neuropsychiatric disorder a pharmaceutical compn. contg. (i) compds. having D4 antagonistic, partial agonistic or inverse agonistic activity and (ii) compds. having 5-HT2A antagonistic, partial agonistic or inverse agonistic, and (iii) any known medicinal compd. and compns. of said compds. The combined D4 and 5-HT2A antagonistic, partial agonistic or inverse agonistic effects may reside within the same chem. or biol. compd. or in two different chem. and/or

biol. compds.
IT **93413-62-8**, Desvenlafaxine
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(use of D4 and 5-HT2A antagonists or inverse agonists or partial agonists in treatment of emotional dysregulation in mental disorders combined with other agents)
RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2005:735104 HCAPLUS
DOCUMENT NUMBER: 143:199895
TITLE: Multiparticulate O-desmethylvenlafaxine salts and uses thereof
INVENTOR(S): Diorio, Christopher Richard; Shah, Syed M.; Fawzi, Mahdi B.
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

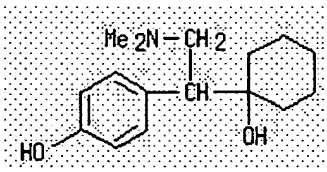
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005175698	A1	20050811	US 2005-42436	20050125
WO 2005077340	A1	20050825	WO 2005-US2215	20050125

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-542384P P 20040206

AB A multiparticulate O-desmethylvenlafaxine (ODV) succinate or formate is described. Methods of treating depression and reducing the gastrointestinal side-effects of ODV are also described.
IT **93413-62-8D**, O-Desmethylvenlafaxine, salts **448904-47-0** **861972-83-0**
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(multiparticulate O-desmethylvenlafaxine salts and uses thereof)

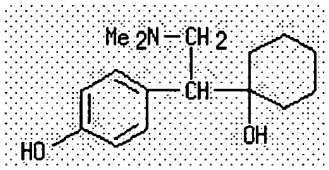
RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



RN 448904-47-0 HCAPLUS
CN Butanedioic acid, compd. with 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol (1:1) (9CI) (CA INDEX NAME)

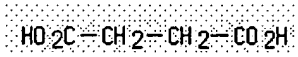
CM 1

CRN 93413-62-8
CMF C16 H25 N O2



CM 2

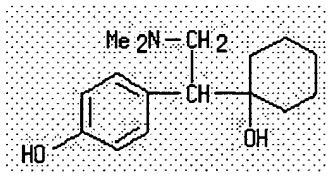
CRN 110-15-6
CMF C4 H6 O4



RN 861972-83-0 HCAPLUS
CN Formic acid, compd. with 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol (1:1) (9CI) (CA INDEX NAME)

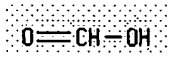
CM 1

CRN 93413-62-8
CMF C16 H25 N O2



CM 2

CRN 64-18-6
CMF C H2 O2



L4 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | More References

ACCESSION NUMBER: 2005:588665 HCAPLUS
DOCUMENT NUMBER: 143:103256
TITLE: Combination of a sedative and a neurotransmitter modulator for improving sleep quality and treating depression
INVENTOR(S): Lalji, Karim; Barberich, Timothy J.; Caron, Judy; Wessel, Thomas
PATENT ASSIGNEE(S): Sepracor Inc., USA
SOURCE: PCT Int. Appl., 394 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005060968	A1	20050707	WO 2004-US40962		20041208
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2005176680	A1	20050811	US 2004-7795		20041208
PRIORITY APPLN. INFO.:			US 2003-529156P	P	20031211
			US 2004-541614P	P	20040204
			US 2004-633213P	P	20041203

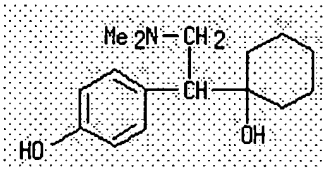
AB One aspect of the present invention relates to pharmaceutical compns. contg. 2 or more active agents that when taken together can be used to treat, e.g., insomnia and/or depression. The first component of the pharmaceutical compn. is a GABA receptor modulating compd. The second component of the pharmaceutical compn. is a serotonin reuptake inhibitor (SRI), a norepinephrine reuptake inhibitor (NRI), a 5-HT2A modulator, or dopamine reuptake inhibitor (DRI). In certain embodiments, the pharmaceutical compn. comprises eszopiclone. In a preferred embodiment, the pharmaceutical compn. comprises eszopiclone and fluoxetine. The present invention also relates to a method of treating a sleep abnormality, treating insomnia, treating depression, augmenting antidepressant therapy, eliciting a dose-sparing effect, reducing depression relapse, improving the efficacy of antidepressant therapy or improving the tolerability of antidepressant therapy, comprising co-administering to a patient in need thereof a GABA-receptor-modulating compd.; and a SRI, NRI, 5-HT2A modulator or DRI. Co-administration of eszopiclone with fluoxetine was well-tolerated and assocd. with rapid, sustained improvement in sleep and daytime symptoms in patients with MDD and insomnia. The rapid sleep improvement with adjunctive eszopiclone may be important, given the relatively slower onset of antidepressant effects with SSRIs.

IT **93413-62-8** **142761-11-3** **142761-12-4**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(combination of sedative and neurotransmitter modulator for improving sleep quality and treating depression)

RN 93413-62-8 HCAPLUS

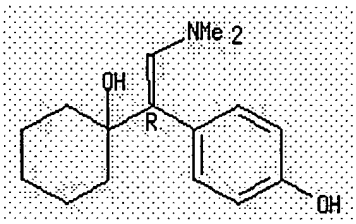
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



RN 142761-11-3 HCAPLUS

CN Phenol, 4-[(1R)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

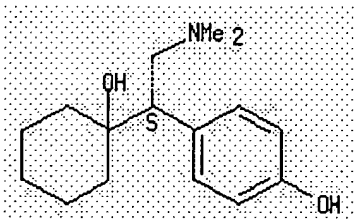
Absolute stereochemistry. Rotation (-).



RN 142761-12-4 HCAPLUS

CN Phenol, 4-[(1S)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2005:517402 HCAPLUS
DOCUMENT NUMBER: 143:38422
TITLE: Combination therapy for dementia, depression and apathy
INVENTOR(S): Sheldon, Leslie James
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005053703 A1 20050616 WO 2004-CA2071 20041202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

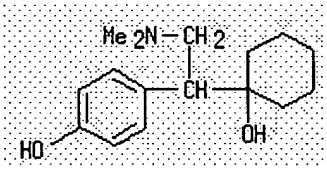
PRIORITY APPLN. INFO.: US 2003-526137P P 20031202

AB The invention provides compns. and kits for treating dementia, depression and apathy using combination therapy involving either a monoamine oxidase inhibitor or a selective serotonin reuptake inhibitor in combination with an anti-psychotic agent.

IT **93413-62-8**, Desvenlafaxine
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combination therapy for dementia, depression and apathy)

RN 93413-62-8 HCAPLUS

CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2005:516281 HCAPLUS
DOCUMENT NUMBER: 143:38421
TITLE: Use of D4 and 5-HT2A antagonists, inverse agonists or partial agonists
INVENTOR(S): Buntinx, Erik
PATENT ASSIGNEE(S): B&B Beheer N. V., Belg.
SOURCE: Eur. Pat. Appl., 145 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1541197	A1	20050615	EP 2004-25035	20041021
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
EP 1547650	A1	20050629	EP 2003-447279	20031202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
EP 1576985	A1	20050921	EP 2004-447066	20040318
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK

JP 2005194263	A2	20050721	JP 2004-349085 20041104
US 2005203130	A1	20050915	US 2004-984683 20041109
CA 2487529	AA	20050602	CA 2004-2487529 20041115
WO 2005053796	A1	20050616	WO 2004-BE172 20041202

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

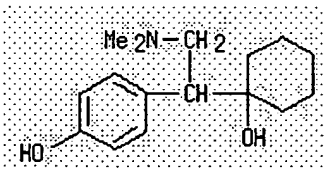
EP 2003-447279	A	20031202
EP 2004-447001	A	20040105
EP 2004-447066	A	20040318
CA 2003-2451798	A	20031202
US 2003-725965	A2	20031202
US 2004-752423	A2	20040106
CA 2004-2461248	A	20040318
US 2004-803793	A2	20040318
EP 2004-25035	A	20041021
JP 2004-349085	A	20041104
US 2004-984683	A	20041109
CA 2004-2487529	A	20041115

AB The present invention relates to the use of compds. and compns. of compds. having D4 and 5-HT2A antagonistic, partial agonistic or inverse agonistic activity for the treatment of the underlying dysregulation of the emotional functionality of mental disorders (i.e. affect instability-hypersensitivity-hyperesthesia-dissociative phenomena-etc.). The invention also relates to methods comprising administering to a patient diagnosed as having a neuropsychiatric disorder a pharmaceutical compn. contg. (i) compds. having D4 antagonistic, partial agonistic or inverse agonistic activity and (ii) compds. having 5-HT2A antagonistic, partial agonistic or inverse agonistic, and (iii) any known medicinal compd. and compns. of said compds. The combined D4 and 5-HT2A antagonistic, partial agonistic or inverse agonistic effects may reside within the same chem. or biol. compd. or in two different chem. and/or biol. compds.

IT **93413-62-8**, Desvenlafaxine
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(use of D4 and 5-HT2A antagonists or inverse agonists or partial agonists in treatment of emotional dysregulation in mental disorders combined with other agents)

RN 93413-62-8 HCAPLUS

CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Chart | References

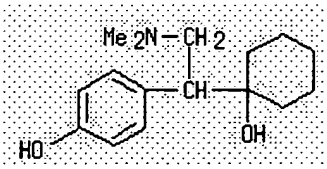
ACCESSION NUMBER: 2005:493467 HCAPLUS
DOCUMENT NUMBER: 143:38409
TITLE: Combination drug therapy to treat obesity
INVENTOR(S): Seed, John C.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051297	A2	20050609	WO 2004-US38981	20041119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005143350	A1	20050630	US 2004-993496	20041118
PRIORITY APPLN. INFO.:			US 2003-523610P	P 20031119
			US 2004-993496	A 20041118

AB Provided are methods of achieving desirable wt. loss in an overweight or obese individual by administering at least one anticholinesterase agent and at least one antidepressant. The invention also provides for pharmaceutical compns. and kits for simultaneous delivery of at least one anticholinesterase agent and at least one antidepressant.

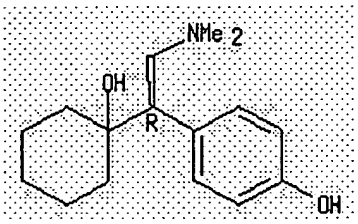
IT **93413-62-8**, Desvenlafaxine **142761-11-3**
142761-12-4
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combination drug therapy to treat obesity)

RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



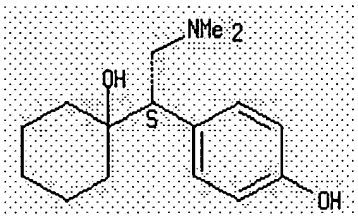
RN 142761-11-3 HCAPLUS
CN Phenol, 4-[(1R)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 142761-12-4 HCAPLUS
CN Phenol, 4-[(1S)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L4 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Other References

ACCESSION NUMBER: 2005:369266 HCAPLUS
DOCUMENT NUMBER: 142:404276
TITLE: Method using adrenergic α2B antagonists, alone or in combination with norepinephrine reuptake inhibitors or dual norepinephrine/serotonin reuptake inhibitors for treating vasomotor symptoms
INVENTOR(S): Deecher, Darlene Coleman; Beyer, Chad Edward; Leventhal, Liza
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037260	A2	20050428	WO 2004-US33754	20041013
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004152710	A1	20040805	US 2003-685812	20031014
WO 2004035058	A1	20040429	WO 2003-US32759	20031015
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM,				

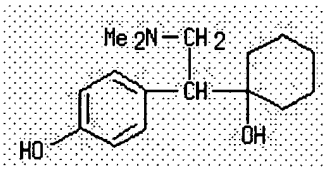
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005130987	A1	20050616	US 2004-962897		20041012
PRIORITY APPLN. INFO.:			US 2003-510897P	P	20031014
			US 2003-685812	A	20031014
			WO 2003-US32759	A	20031015
			US 2004-962897	A	20041012
			US 2002-418591P	P	20021015

AB The invention discloses selective adrenergic α2B antagonists alone, selective adrenergic α2B antagonists in combination with norepinephrine reuptake inhibitors (NRI) (as a single compd. or as a combination of two or more compds.), or selective adrenergicα2B antagonists in combination with dual norepinephrine reuptake inhibitors/serotonin reuptake inhibitors (NRI/SRI) (as a single compd. or as a combination of two or more compds.) and methods of their use in the treatment of vasomotor symptoms.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adrenergic α2B antagonists, alone or in combination with norepinephrine reuptake inhibitors or dual norepinephrine/serotonin reuptake inhibitors for treating vasomotor symptoms)

RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2005:340220 HCAPLUS
DOCUMENT NUMBER: 142:360912
TITLE: Extended release pharmaceutical dosage form
INVENTOR(S): Heaton, Nicholas; Potts, Angela; Armstrong, Ian; Provost, James Andrew
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1523979	A1	20050420	EP 2003-256438	20031013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
WO 2005039527	A2	20050506	WO 2004-EP11339	20041011

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

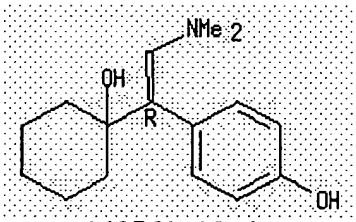
US 2005129762 A1 20050616 US 2004-964012 20041013
PRIORITY APPLN. INFO.: EP 2003-256438 A 20031013

AB This invention relates to novel extended release pharmaceutical dosage forms for orally delivering drugs to mammals, e.g., humans. More particularly, this invention concerns novel dosage forms of water sol. drugs such as venlafaxine, enantiomeric (R or S) forms of venlafaxine, metabolites of venlafaxine such as O-desmethyl venlafaxine (ODV) or enantiomeric (R or S) forms of said metabolites which dosage forms have an extended release profile when taken orally. This invention also provides processes for prepg. such dosage forms and methods of using them. For example, extended-release tablets of venlafaxine hydrochloride comprised (1) a tablet core contg. venlafaxine HCl 81.45, stearic acid 96.55, microcryst. cellulose 20, colloidal silica 0.4, Mg stearate 1.6 mg and (2) a coating layer contg. venlafaxine HCl 3.89 and stearic acid 16.97 mg.

IT **142761-11-3**, (-)-O-DesmethylVenlafaxine **142761-12-4**, (+)-O-DesmethylVenlafaxine
RL: PKT (Pharmacokinetics); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(extended release oral dosage forms of venlafaxine enantiomers and metabolites)

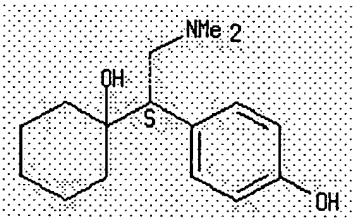
RN 142761-11-3 HCAPLUS
CN Phenol, 4-[(1R)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 142761-12-4 HCAPLUS
CN Phenol, 4-[(1S)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

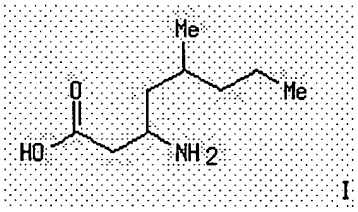
Full Text | Other References

ACCESSION NUMBER: 2005:238701 HCAPLUS
DOCUMENT NUMBER: 142:316826
TITLE: A preparation of combinations comprising alpha-2-delta ligands and dual serotonin-noradrenaline reuptake inhibitors, useful for treatment of pain
INVENTOR(S): Dooley, David James; Field, Mark John; Williams, Richard Griffith
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 23 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005059715	A1	20050317	US 2004-935824	20040908
WO 2005025675	A1	20050324	WO 2004-IB2943	20040906

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-502556P P 20030912
GI



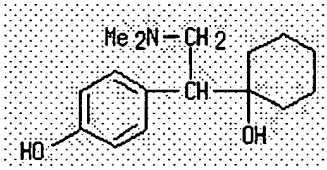
I

AB The invention relates to a combination, particularly a synergistic combination, of an alpha-2-delta ligand and a dual serotonin-noradrenaline reuptake inhibitor (DSNRI) or one or both of a selective serotonin reuptake inhibitor (SSRI) and a selective noradrenaline reuptake inhibitor (SNRI), and pharmaceutically acceptable salts thereof, pharmaceutical compns. thereof and their use in the treatment of pain, particularly neuropathic pain (no biol. data). For instance, 3-amino-5-methyloctanoic acid hydrochloride (I?HCl) was prepd. from (S)-citronellyl bromide in eight steps.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(dual serotonin-noradrenaline reuptake inhibitor; pharmaceutical combinations comprising alpha-2-delta ligands and dual serotonin-noradrenaline reuptake inhibitors)

RN 93413-62-8 HCAPLUS

CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 11 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

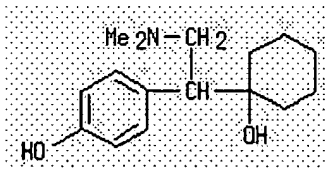
Full Text | Citing References

ACCESSION NUMBER: 2005:105997 HCAPLUS
DOCUMENT NUMBER: 142:328916
TITLE: QSAR treatment of drugs transfer into human breast milk
AUTHOR(S): Katritzky, Alan R.; Dobchev, Dimitar A.; Huer, Evrim; Fara, Dan C.; Karelson, Mati
CORPORATE SOURCE: Center for Heterocyclic Compounds, Department of Chemistry, University of Florida, Gainesville, FL, 32611, USA
SOURCE: Bioorganic & Medicinal Chemistry (2005), 13(5), 1623-1632
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A satisfactory model is developed using for the correlation and prediction of milk to plasma concn. ratios (M/P ratio) for diverse pharmaceuticals. A set of exptl. derived M/P ratio values were collected from the literature for 115 widely used pharmaceuticals. The exptl. logarithmic M/P ratios were tested with more than 850 theor. mol. descriptors including constitutional, topol., geometrical, quantum chem., thermodn., and electrostatic types. Based on the data set, for 100 commonly used drugs, a seven-parameter QSAR model was derived that shows a satisfactory (R2 = 0.791) correlation between predicted and obsd. values of log (M/P) ratio.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: PAC (Pharmacological activity); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(QSAR treatment of drug transfer into human breast milk)

RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 126 THERE ARE 126 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

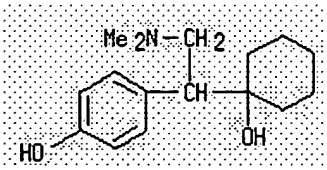
Full Text | Citing References

ACCESSION NUMBER: 2005:68165 HCAPLUS
DOCUMENT NUMBER: 143:19763
TITLE: Combination therapy with venlafaxine and carbamazepine in depressive patients not responding to venlafaxine: pharmacokinetic and clinical aspects
AUTHOR(S): Ciusani, Elio; Zullino, Daniele F.; Eap, Chin B.; Brawand-Amey, Marlyse; Brocard, Murielle; Baumann, Pierre
CORPORATE SOURCE: Unite de Biochimie et Psychopharmacologie Clinique, Departement Universitaire de Psychiatrie Adulte, Prilly-Lausanne, Switz.
SOURCE: Journal of Psychopharmacology (London, United Kingdom) (2004), 18(4), 559-566
CODEN: JOPSEQ; ISSN: 0269-8811
PUBLISHER: Sage Publications Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The chiral antidepressant venlafaxine (VEN) is both a serotonin and a norepinephrine uptake inhibitor. CYP2D6 and CYP3A4 contribute to its metab., which has been shown to be stereoselective. Ten CYP2D6 genotyped and depressive (F32x and F33x, ICD-10) patients participated in an open study on the pharmacokinetic and pharmacodynamic consequences of a carbamazepine augmentation in VEN non-responders. After an initial 4-wk treatment with VEN (195 ? 52 mg/day), the only poor metabolizer out of 10 depressive patients had the highest plasma concns. of S-VEN and R-VEN, resp., whereas those of R-O-dimethyl-VEN were lowest. Five non-responders completed the second 4-wk study period, during which they were submitted to a combined VEN-carbamazepine treatment. In the only non-responder to this combined treatment, there was a dramatic decrease of both enantiomers of VEN, O-dimethylvenlafaxine, N-desmethylvenlafaxine and N,O-didesmethylvenlafaxine in plasma, which suggests non-compliance, although metabolic induction by carbamazepine cannot entirely be excluded. The administration of carbamazepine [mean ? SD, range: 360 ? 89 (200-400) mg/day] over 4 wk did not result in a significant modification of the plasma concns. of the enantiomers of VEN and its O- and N-demethylated metabolites in the other patients. In conclusion, these preliminary observations suggest that the combination of VEN and carbamazepine represents an interesting augmentation strategy by its efficacy, tolerance and absence of pharmacokinetic modifications. However, these findings should be verified in a more comprehensive study.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmacokinetics showed that carbamazepine did not significantly change plasma concn. of venlafaxine enantiomer R-VEN and S-VEN in depressive patient not responding to VEN)

RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Cited References

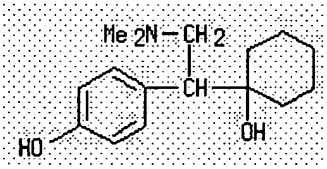
ACCESSION NUMBER: 2004:1035019 HCAPLUS
DOCUMENT NUMBER: 142:11574
TITLE: Therapeutic compositions including resin-loaded bioavailability enhancers
INVENTOR(S): Hughes, Lyn
PATENT ASSIGNEE(S): Rohm and Haas Company, USA
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1481690	A1	20041201	EP 2004-252933	20040518
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2004359665	A2	20041224	JP 2004-29032	20040205
US 2004241135	A1	20041202	US 2004-854906	20040527
PRIORITY APPLN. INFO.:			US 2003-474663P	P 20030530

AB The present invention relates to a resin comprising a bio-enhancer and an optional therapeutically active ingredient or precursor thereof loaded thereon. The bio-enhancer is ionizable or non-ionizable, and the resin may be a cation exchange resin or an anion exchange resin. For example, resin loaded with both active ingredient and bioenhancers was produced by mixing O-desmethylvenlafaxine with strongly basic anion exchange resin ethanol solns., followed by adding succinic acid and then filtered and dried to obtain the resinate contg. O-desmethylvenlafaxine succinate.

IT **93413-62-8**, o-Desmethyl venlafaxine
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(therapeutic compns. contg. resin-loaded bioavailability enhancers and therapeutic agents)

RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

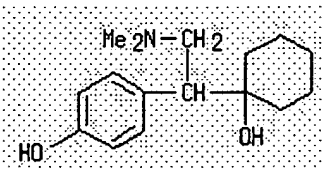


IT **448904-47-0P**
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(therapeutic compns. contg. resin-loaded bioavailability enhancers and therapeutic agents)

RN 448904-47-0 HCAPLUS
CN Butanedioic acid, compd. with 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol (1:1) (9CI) (CA INDEX NAME)

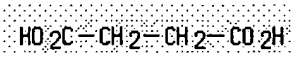
CM 1

CRN 93413-62-8
CMF C16 H25 N O2



CM 2

CRN 110-15-6
CMF C4 H6 O4



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Cited References

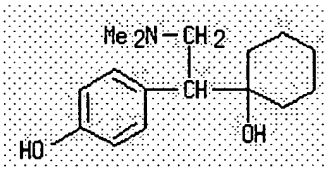
ACCESSION NUMBER: 2004:635508 HCAPLUS
DOCUMENT NUMBER: 142:69012
TITLE: A pilot study of newer antidepressant concentrations in cord and maternal serum and possible effects in the neonate
AUTHOR(S): Rampono, Jonathan; Proud, Stephen; Hackett, L. Peter; Kristensen, Judith H.; Ilett, Kenneth F.
CORPORATE SOURCE: Department of Psychological Medicine, Women's and Children's Health Service Subiaco, Subiaco, 6008, Australia
SOURCE: International Journal of Neuropsychopharmacology (2004), 7(3), 329-334
CODEN: IJNUFB; ISSN: 1461-1457
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Antidepressants are often used antenatally, and placental transfer may lead to adverse effects (toxicity) in the neonate. Pregnant women taking fluoxetine (n=4), sertraline (n=4), paroxetine (n=2) or venlafaxine (n=1) in the last trimester were studied. Maternal and cord sera were collected at delivery and infant serum on day 5 after birth for measurement of antidepressant concns. Neonatal Abstinence Scores (NAS) were measured in the infants on days 1-3 after birth. In maternal serum, median drug concns. were: fluoxetine (96 μg/l), norfluoxetine (110 μg/l), sertraline (11 μg/l), desmethylsertraline (38 μg/l), paroxetine (mean 12 μg/l), venlafaxine (220 μg/l), and O-desmethylvenlafaxine (392 μg/l). Corresponding median values in cord serum were: fluoxetine (65 μg/l), norfluoxetine (81 μg/l), sertraline (10 μg/l), desmethylsertraline (27 μg/l), paroxetine (mean 6 μg/l), venlafaxine (232 μg/l), and O-desmethylvenlafaxine (406 μg/l). Corresponding median cord:maternal concn. ratios were 0.67 for fluoxetine and 0.72 for norfluoxetine, 0.67 for sertraline and 0.63 for demethylsertraline, 0.52 (mean) for paroxetine, and 1.1 and 1.0 for venlafaxine and O-desmethylvenlafaxine resp. The neonates of two patients taking

fluoxetine had high NAS. Only fluoxetine and norfluoxetine were detected in infant serum. Our data show substantial placental transfer of antidepressants, but only fluoxetine persisted in the infant's serum. Neonatal toxicity may be assocd. with serotonin uptake blockade, and also be influenced by neonatal clearance.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antidepressant infusion showed effective substantial placental transfer of methylvenlafaxine, showed no persistence in infant serum leading to neonatal toxicity indicating assocn. of serotonin re-uptake blockade and neonatal clearance)

RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | More References

ACCESSION NUMBER: 2004:354797 HCAPLUS
DOCUMENT NUMBER: 140:350606
TITLE: Use of norepinephrine reuptake modulators for preventing and treating vasomotor symptoms
INVENTOR(S): Deecher, Darlene Coleman; Merchenthaler, Istvan Joseph; Leventhal, Liza; Sipe, Kimberly Jean; O'Connor, Lawrence Thomas
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035058	A1	20040429	WO 2003-US32759	20031015
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004152710	A1	20040805	US 2003-685812	20031014
CA 2502032	AA	20040429	CA 2003-2502032	20031015
EP 1551413	A1	20050713	EP 2003-774853	20031015

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

BR 2003015355	A	20050823	BR 2003-15355 20031015
US 2005130987	A1	20050616	US 2004-962897 20041012
WO 2005037260	A2	20050428	WO 2004-US33754 20041013

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

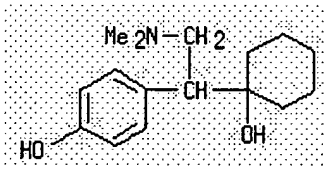
PRIORITY APPLN. INFO.:

US 2002-418591P	P	20021015
US 2003-685812	A	20031014
US 2003-510897P	P	20031014
WO 2003-US32759	W	20031015
US 2004-962897	A	20041012

AB The invention discloses the use of compds. and compn. of compds. that modulate norepinephrine levels for the prevention and treatment of vasomotor symptoms, such as hot flush, caused by, inter alia, thermoregulatory dysfunctions. Compds. of the invention include e.g. desipramine.

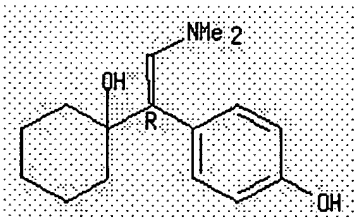
IT **93413-62-8**, DVS 233 **142761-11-3** **142761-12-4**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(norepinephrine reuptake modulators for preventing and treating vasomotor symptoms)

RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



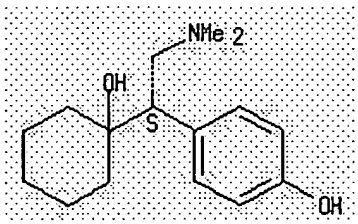
RN 142761-11-3 HCAPLUS
CN Phenol, 4-[(1R)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 142761-12-4 HCAPLUS
CN Phenol, 4-[(1S)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:354778 HCAPLUS
DOCUMENT NUMBER: 140:350603
TITLE: A method of treating vasomotor symptoms using a compound having norepinephrine reuptake inhibitor activity and 5-HT2a antagonistic activity
INVENTOR(S): Deecher, Darlene Coleman; Merchenthaler, Istvan Joseph
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035036	A1	20040429	WO 2003-US32554	20031015
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004180879	A1	20040916	US 2003-685974	20031014
CA 2502027	AA	20040429	CA 2003-2502027	20031015
EP 1551380	A1	20050713	EP 2003-774828	20031015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015346	A	20050823	BR 2003-15346	20031015
PRIORITY APPLN. INFO.:			US 2002-418516P	P 20021015
			US 2003-685974	A 20031014
			WO 2003-US32554	W 20031015

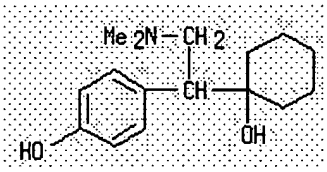
AB The invention discloses the use of compds. and compns. of compds. that modulate norepinephrine levels for the treatment of vasomotor symptoms, e.g. thermoregulatory disorders. The invention also discloses the use of compds. and compns. of compds. having norepinephrine reuptake inhibitor (NRI) activity alone or norepinephrine reuptake inhibitor and serotonin reuptake inhibitor (NRI/SRI) dual activity in combination with 5-HT2a receptor antagonist activity.

IT **93413-62-8**, Desvenlafaxine
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(compds. with norepinephrine reuptake inhibitor activity and 5-HT2a antagonistic activity for treatment of vasomotor symptoms)

RN 93413-62-8 HCAPLUS

CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

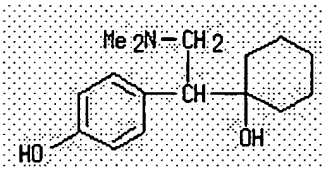
Full Text | Citing References

ACCESSION NUMBER: 2004:354777 HCAPLUS
DOCUMENT NUMBER: 140:350602
TITLE: Use of norepinephrine reuptake modulators for preventing and treating vasomotor symptoms
INVENTOR(S): Deecher, Darlene Coleman; Merchenthaler, Istvan Joseph; Leventhal, Liza; Sipe, Kimberly Jean; O'Connor, Lawrence Thomas
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035035	A1	20040429	WO 2003-US32760	20031015
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004143008	A1	20040722	US 2003-684777	20031014
CA 2502021	AA	20040429	CA 2003-2502021	20031015
EP 1551379	A1	20050713	EP 2003-774854	20031015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015314	A	20050816	BR 2003-15314	20031015
PRIORITY APPLN. INFO.:			US 2002-418591P	P 20021015
			US 2003-684777	A 20031014
			WO 2003-US32760	W 20031015

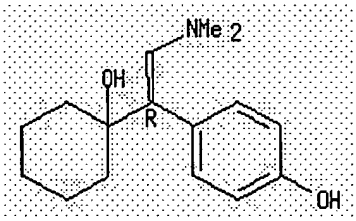
AB The invention discloses the use of compds. and compns. of compds. that modulate norepinephrine levels for the prevention and treatment of vasomotor symptoms, e.g. hot flush, caused by, inter alia, thermoregulatory dysfunctions. Compds. of the invention include e.g. venlafaxine.

IT **93413-62-8**, DVS 233 **142761-11-3** **142761-12-4**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(norepinephrine reuptake modulators for preventing and treating vasomotor symptoms)
RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



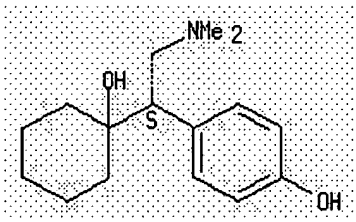
RN 142761-11-3 HCAPLUS
CN Phenol, 4-[(1R)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 142761-12-4 HCAPLUS
CN Phenol, 4-[(1S)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:181965 HCAPLUS
DOCUMENT NUMBER: 140:205161
TITLE: Pharmaceutical preparations comprising a 5HT uptake inhibitor and a homopolymer or copolymer of N-vinylpyrrolidone
INVENTOR(S): Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra
PATENT ASSIGNEE(S): Cipla Limited, India
SOURCE: Brit. UK Pat. Appl., 13 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

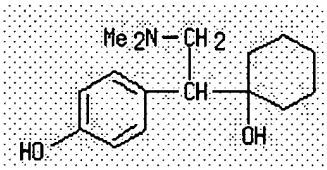
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2392385	A1	20040303	GB 2002-20334	20020902

PRIORITY APPLN. INFO.: GB 2002-20334 20020902

AB Pharmaceutically acceptable prepns. are described comprising one or more 5HT uptake inhibitors with an excipient matrix comprising a homopolymer or copolymer of N-vinylpyrrolidone in which the 5HT uptake inhibitors are complexed with the homopolymer or copolymer. The 5HT uptake inhibitors are preferably in amorphous form and may be selected from citalopram, venlafaxine, desmethyl venlafaxine, sertraline, fluoxetine and their salts. The homopolymer or copolymer is preferably a polyvinylpyrrolidone or crospovidone. The prepns. are suitable for the treatment of a range of diseases which are prevented, ameliorated or eliminated by the administration of a 5HT uptake inhibitor. Such diseases include depression, substance abuse and senile dementia. One or more 5HT uptake inhibitors together with a homopolymer or copolymer of N-vinylpyrrolidone may be used in the treatment of such diseases. For example, to a soln. of 25 g of citalopram in 125 mL of ethanol was added 75 g of polyvinylpyrrolidone K30 at room temp. to obtain a clear soln. The soln. was concd. under vacuum at a temp. below 40? to give an amorphous solid, which was filtered off. The amt. of citalopram in the complex was 22% to 28%.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(solid oral compns. comprising 5HT uptake inhibitor and vinylpyrrolidone polymer)

RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

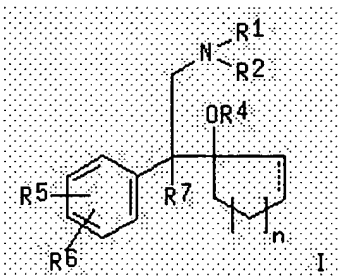
Full Text | Cited References

ACCESSION NUMBER: 2003:931155 HCAPLUS
DOCUMENT NUMBER: 139:391365
TITLE: Methods of treating gastrointestinal and genitourinary pain disorders using venlafaxine and derivatives
INVENTOR(S): Karlstadt, Robyn Gail; Lynn, Richard Brian; Burton, Michael Scott; Danilewitz, Mervyn
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003097029	A1	20031127	WO 2003-US15230	20030515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2485736	AA	20031127	CA 2003-2485736	20030515
US 2004019101	A1	20040129	US 2003-438572	20030515
BR 2003010083	A	20050215	BR 2003-10083	20030515
EP 1505960	A1	20050216	EP 2003-753036	20030515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005530779	T2	20051013	JP 2004-505028	20030515
PRIORITY APPLN. INFO.:			US 2002-381305P	P 20020517
			WO 2003-US15230	W 20030515

OTHER SOURCE(S): MARPAT 139:391365
GI

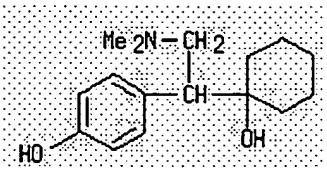


AB The invention provides a method of treating functional gastrointestinal and genitourinary disorders in a mammal by administering to the mammal an effective amt. of hydroxycycloalkane phenethylamine I where the dotted line represents optional unsatn.; R1, R7 = H, alkyl; R2 = alkyl; R4 = H, alkyl, formyl, alkanol; R5, R6 = H, OH, alkyl, alkoxy, alkanoyloxy, cyano, nitro, alkylmercapto, amino, alkylamino, dialkylamino, alkanamido, halo, trifluoromethyl, or, taken together, methylenedioxy; n is [0-4], or a pharmaceutically acceptable salt thereof.

IT **93413-62-8**, O-DesmethylVenlafaxine
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(venlafaxine and derivs. for treatment of gastrointestinal and genitourinary pain disorders)

RN 93413-62-8 HCAPLUS

CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Cited References

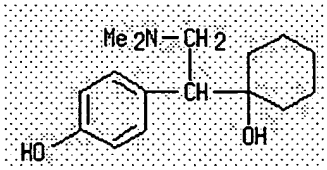
ACCESSION NUMBER: 2003:752480 HCAPLUS
DOCUMENT NUMBER: 140:245936
TITLE: A High-Performance Liquid Chromatography Method with Photodiode-Array UV Detection for Therapeutic Drug Monitoring of the Nontricyclic Antidepressant Drugs
AUTHOR(S): Duverneuil, Charlotte; de la Grandmaison, Geoffroy Lorin; de Mazancourt, Philippe; Alvarez, Jean-Claude
CORPORATE SOURCE: Laboratoire de Pharmacologie-Toxicologie and Service de Medecine Legale, Centre Hospitalier Universitaire Raymond Poincare, Garches, 92380, Fr.
SOURCE: Therapeutic Drug Monitoring (2003), 25(5), 565-573
CODEN: TDMODV; ISSN: 0163-4356
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new rapid and sensitive high-performance liq. chromatog. method has been developed for the screening and detn. in human plasma of the 11 most commonly prescribed non-tricyclic antidepressants and two metabolites: fluoxetine, norfluoxetine, sertraline, paroxetine, citalopram, fluvoxamine, moclobemide, mirtazapine, milnacipram, toloxatone, venlafaxine, desmethyl venlafaxine, and viloxazine. It involves liq.-liq. extn. procedures followed by liq. chromatog. coupled to photodiode-array UV detection with three fixed wavelengths (220, 240, and 290 nm). Compds. were sepd. on a 5-μm Hypurity C18 (ThermoHypersil) analytic column (250 4.6 ı mm i.d.) using a gradient of acetonitrile-phosphate buffer pH 3.8 at a flow rate of 1.0 mL/min. The total anal. time was only 18 min per sample. Extn. recoveries were in the 74-109% range for 11 compds. but were of only 59% for moclobemide and less than 10% for toloxatone. Calibration curves were linear in the 25 to 1000 ng/mL range for all compds., all of them with coeffs. of detn. (r2 values) ? 0.999. Limits of detection (LODs) ranged from 2.5 to 5 ng/mL except for toloxatone (10 ng/mL). Intra-assay and inter-assay precision and accuracy were studied at two concn. levels (50 and 500 ng/mL). The intra-assay coeffs. of variation (CVs) for all compds. were ? 7.6%, and all inter-assay CVs were below 11.5% except for milnacipram (14.8%). The intra-assay and inter-assay accuracies for all compds. were found to be within 88.4% and 105.9% at 50 ng/mL and within 87.2% and 100.5% at 500 ng/mL. The performance of the method allows the therapeutic drug monitoring of the most prescribed non-tricyclic antidepressant drugs as well as its use in toxicol. screening.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: ANT (Analyte); BSU (Biological study, unclassified); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); USES (Uses)
(metabolite; HPLC method with photodiode-array UV detection for therapeutic drug monitoring of the non-tricyclic antidepressant drugs)

RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA

INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Cited References

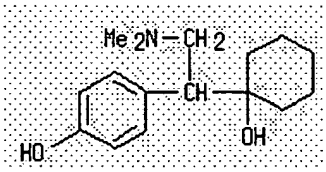
ACCESSION NUMBER: 2003:584504 HCAPLUS
DOCUMENT NUMBER: 140:172
TITLE: Analysis of eighteen antidepressants, four atypical antipsychotics and active metabolites in serum by liquid chromatography: a simple tool for therapeutic drug monitoring
AUTHOR(S): Frahnert, Christine; Rao, Marie Luise; Grasmader, Katja
CORPORATE SOURCE: Department of Psychiatry, University of Bonn, Bonn, D-53105, Germany
SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2003), 794(1), 35-47
CODEN: JCBAAI; ISSN: 1570-0232
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Therapeutic drug monitoring necessitates efficient, fast and reliable anal. methods validated by external quality control. We therefore devised an isocratic reversed-phase HPLC method with UV detection and optimized this to quantify mirtazapine, reboxetine, moclobemide, venlafaxine, O-desmethylvenlafaxine, paroxetine, fluvoxamine, fluoxetine, norfluoxetine, sertraline, citalopram, amitriptyline, nortriptyline, imipramine, desipramine, doxepin, nordoxepin, clomipramine, norclomipramine, trimipramine, mianserine, maprotiline, normaprotiline, amisulpride, clozapine, norclozapine, quetiapine, risperidone and 9-OH-risperidone in human serum. After solid-phase extn. of the drugs and metabolites, the chromatog. sepn. was achieved on a Nucleosil 100-Protect 1 column with acetonitrile-potassium dihydrogenphosphate buffer as mobile phase. The method was validated for therapeutic and toxic serum ranges. A linear relationship (r>0.998) was obtained between the concn. and the detector signal. Recoveries were between 75 and 99% for the drugs and metabolites. The accuracy of the quality control samples, expressed as percent recovery, ranged from 91 to 118%; intra- and inter-assay-relative std. deviations were 0.9-10.2% and 0.9-9.7%, resp. Addnl. external quality control is carried out since 3 yr. This method is applicable to rapidly and effectively analyze serum or plasma samples for therapeutic drug monitoring of about 30 antidepressants and atypical antipsychotics.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: ANT (Analyte); BSU (Biological study, unclassified); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); USES (Uses)
(anal. of antidepressants and atypical antipsychotics and active metabolites in serum by liq. chromatog. for therapeutic drug monitoring)

RN 93413-62-8 HCAPLUS

CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

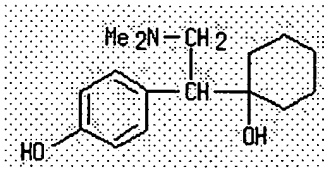
Full Text | Citing References

ACCESSION NUMBER: 2003:262485 HCAPLUS
DOCUMENT NUMBER: 139:207091
TITLE: Inhibition of P-glycoprotein by newer antidepressants
AUTHOR(S): Weiss, Johanna; Dormann, Sven-Maria Gregor; Martin-Facklam, Meret; Kerpen, Christian Johannes; Ketabi-Kiyanvash, Nahal; Haefeli, Walter Emil
CORPORATE SOURCE: Department of Internal Medicine VI, Clinical Pharmacology, and Pharmacoepidemiology, University of Heidelberg, Heidelberg, Germany
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2003), 305(1), 197-204
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pharmacokinetic drug-drug interactions often occur at the level of P-glycoprotein (Pgp). To study possible interactions caused by the newer antidepressants we investigated citalopram, fluoxetine, fluvoxamine, paroxetine, reboxetine, sertraline, and venlafaxine and their major metabolites desmethylcitalopram, norfluoxetine, paroxetine-metabolite (paroxetine-M), desmethylsertraline, N-desmethylvenlafaxine, and O-desmethylvenlafaxine for their ability to inhibit Pgp. Pgp inhibition was studied by a fluorometric assay using calcein-acetoxymethylester as Pgp substrate and two different cell systems: L-MDR1 cells (model for human Pgp) and primary porcine brain capillary endothelial cells (pBCECs, model for the blood-brain barrier). Both cell systems proved to be suitable for the evaluation of Pgp inhibitory potency of drugs. All antidepressants tested except O-desmethylvenlafaxine showed Pgp inhibitory activity with sertraline, desmethylsertraline, and paroxetine being the most potent, comparable with the well known Pgp inhibitor quinidine. In L-MDR1 cells fluoxetine, norfluoxetine, fluvoxamine, reboxetine, and paroxetine-M revealed intermediate Pgp inhibition and citalopram, desmethylcitalopram, venlafaxine, and N-desmethylvenlafaxine were only weak inhibitors. The ranking order was similar in pBCECs. The fact that some of the compds. tested exert Pgp inhibitor effects at similar concns. as quinidine suggests that pharmacokinetic drug-drug interactions between the newer antidepressants and Pgp substrates should now be thoroughly studied in vivo.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antidepressant inhibition of P-glycoprotein in relation to pharmacokinetic drug interactions)

RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:637634 HCAPLUS
DOCUMENT NUMBER: 137:190735
TITLE: Novel succinate salt of O-desmethylvenlafaxine
INVENTOR(S): Hadfield, Anthony Francis; Shah, Syed Muzafar; Winkley, Michael William; Sutherland, Karen Wiggins; Provost, James Andrew; Park, Aeri; Shipplett, Rex Alwyn; Russell, Brenton William; Weber, Beat Theodor
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002064543	A2	20020822	WO 2002-US4103		20020211
WO 2002064543	A3	20021212			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2436668	AA	20020822	CA 2002-2436668		20020211
US 2003045583	A1	20030306	US 2002-73743		20020211
US 6673838	B2	20040106			
EP 1360169	A2	20031112	EP 2002-718949		20020211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2002007157	A	20040217	BR 2002-7157		20020211
CN 1501909	A	20040602	CN 2002-808112		20020211
JP 2004529877	T2	20040930	JP 2002-564477		20020211
NO 2003003538	A	20030811	NO 2003-3538		20030811
US 2004044241	A1	20040304	US 2003-654756		20030904
ZA 2003007116	A	20041213	ZA 2003-7116		20030911
US 2005096479	A1	20050505	US 2004-985292		20041110
PRIORITY APPLN. INFO.:			US 2001-268214P	P	20010212
			US 2001-297963P	P	20010613
			US 2002-73743	A3	20020211

WO 2002-US4103 W 20020211
US 2003-654756 B3 20030904

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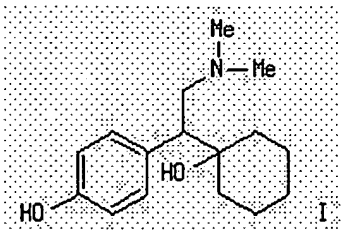
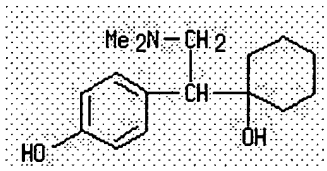


AB A novel salt of O-desmethyl venlafaxine (I) is provided, I succinate. Pharmaceutical compns., dosage forms and methods of use are also provided. Examples are given for the prepn. of I, I monosuccinate and its monohydrate.

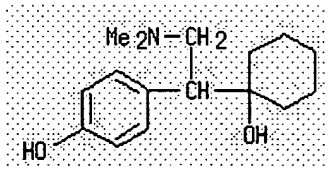
IT **93413-62-8**, O-Desmethylvenlafaxine
RL: PRP (Properties); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(O-desmethylvenlafaxine succinate crystal forms)
RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



IT **386750-22-7P 448904-47-0P**
RL: PRP (Properties); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(O-desmethylvenlafaxine succinate crystal forms)
RN 386750-22-7 HCAPLUS
CN Butanedioic acid, compd. with 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol (1:1), monohydrate (9CI) (CA INDEX NAME)

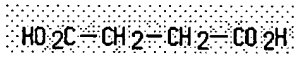
CM 1

CRN 93413-62-8
CMF C16 H25 N O2



CM 2

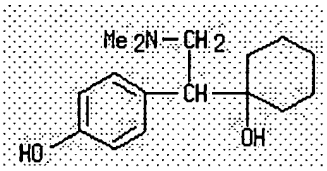
CRN 110-15-6
CMF C4 H6 O4



RN 448904-47-0 HCAPLUS
CN Butanedioic acid, compd. with 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol (1:1) (9CI) (CA INDEX NAME)

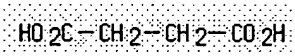
CM 1

CRN 93413-62-8
CMF C16 H25 N O2



CM 2

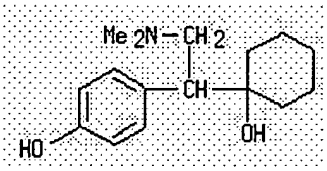
CRN 110-15-6
CMF C4 H6 O4



IT **448904-48-1**
RL: RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(O-desmethylvenlafaxine succinate crystal forms)
RN 448904-48-1 HCAPLUS
CN Butanedioic acid, compd. with 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol (1:2) (9CI) (CA INDEX NAME)

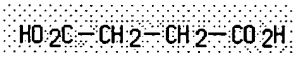
CM 1

CRN 93413-62-8
CMF C16 H25 N O2



CM 2

CRN 110-15-6
CMF C4 H6 O4



L4 ANSWER 24 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:310162 HCAPLUS
DOCUMENT NUMBER: 136:395834
TITLE: Combining bupropion SR with venlafaxine, paroxetine, or fluoxetine: A preliminary report on

pharmacokinetic, therapeutic, and sexual dysfunction effects

AUTHOR(S): Kennedy, Sidney H.; McCann, Sonia M.; Masellis, Mario; McIntyre, Roger S.; Raskin, Joel; McKay, Gordon; Baker, Glen B.

CORPORATE SOURCE: Centre for Addiction and Mental Health, and the Department of Psychiatry, University of Toronto, Toronto, ON, Can.

SOURCE: Journal of Clinical Psychiatry (2002), 63(3), 181-186
CODEN: JCLPDE; ISSN: 0160-6689

PUBLISHER: Physicians Postgraduate Press, Inc.

DOCUMENT TYPE: Journal

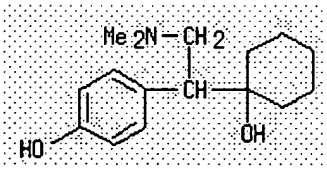
LANGUAGE: English

AB This study was designed to evaluate the effect of combining bupropion sustained release (SR) with venlafaxine, paroxetine, or fluoxetine in patients who reported unacceptable sexual dysfunction when treated with monotherapy with the latter 3 agents. Following a min. of 6 wk of antidepressant treatment with a selective serotonin reuptake inhibitor (SSRI) or venlafaxine (a serotonin-norepinephrine reuptake inhibitor), eligible subjects received a further 8 wk of monitored combination therapy with bupropion SR at a dose of 150 mg/day with no alterations to index antidepressant dosing. There was a clin. significant benefit in 14 (78%) of 18 partial responders or nonresponders, and 33% (N = 6) achieved a full response ($\chi 2$ = 8.06, df = 2, p =.017). Sexual dysfunction, particularly a decrease in orgasmic delay, was also significantly improved with combination therapy (men: paired t = -2.1, df = 6, p =.08; women: paired t = -3.0, df = 7, p =.02). Plasma monitoring of drugs and their metabolites revealed a statistically significant increase in venlafaxine levels (F = 6.89, df = 4,24; p =.001) accompanied by a decrease in O-desmethyl-venlafaxine (F = 14.26; df = 4,24; p <.0005) during combined treatment with bupropion SR. There were no statistically significant changes in plasma levels of SSRIs (paroxetine and fluoxetine) during the trial. Bupropion had an effect on the pharmacokinetics of venlafaxine but not those of the SSRIs. Further investigation of combination treatments under randomized, double-blind conditions is recommended.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(bupropion SR with venlafaxine, paroxetine, or fluoxetine in sexual dysfunction patients with previous monotherapy treatment)

RN 93413-62-8 HCAPLUS

CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

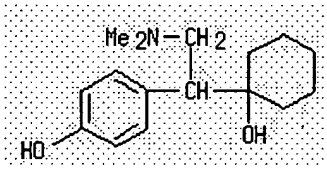
L4 ANSWER 25 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:248775 HCAPLUS

DOCUMENT NUMBER: 136:318772

TITLE: False-positive phencyclidine immunoassay results caused by venlafaxine and O-desmethylvenlafaxine
AUTHOR(S): Sena, Salvador F.; Kazimi, Syed; Wu, Alan H. B.
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Danbury Hospital, Danbury, CT, 06810, USA
SOURCE: Clinical Chemistry (Washington, DC, United States) (2002), 48(4), 676-677
CODEN: CLCHAU; ISSN: 0009-9147
PUBLISHER: American Association for Clinical Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors believe that the data strongly implicate venlafaxine and O-desmethylvenlafaxine as the agents responsible for the false-pos. phencyclidine results the authors obsd. with the RapidTest device.
IT **93413-62-8**, O-Desmethylvenlafaxine
RL: ARU (Analytical role, unclassified); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); USES (Uses)
(phencyclidine false-pos. immunoassay results caused by venlafaxine and O-desmethylvenlafaxine)
RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
Full Text | Links | References

ACCESSION NUMBER: 2002:143294 HCAPLUS
DOCUMENT NUMBER: 136:189323
TITLE: Preparation and pharmaceutical formulation of enantiomers of O-desmethyl venlafaxine
INVENTOR(S): Yardley, John P.; Asselin, Andre A.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp., Cont. of U.S. Ser. No. 590,741, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002022662	A1	20020221	US 2001-957908		20010921
US 2002161055	A1	20021031	US 2002-154994		20020523
US 2003149112	A1	20030807	US 2003-373145		20030224
US 2004176468	A1	20040909	US 2004-799321		20040312
US 2005256206	A1	20051117	US 2005-183573		20050718
PRIORITY APPLN. INFO.:			US 1999-183029P	P	19990615
			US 2000-590741	B1	20000608
			US 2001-957908	A1	20010921
			US 2002-154994	B1	20020523

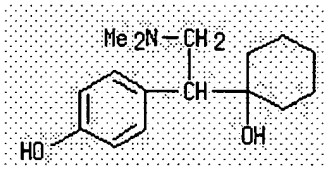
US 2003-373145 A1 20030224
US 2004-799321 B1 20040312

AB This invention provides pharmaceutically active enantiomers of the venlafaxine metabolite O-Desmethyl venlafaxine, R(-)-4-[2-(Dimethylamnino)-1-(1-hydroxycyclo-hexyl)ethyl]phenol or R(-)1-[2-(dimethylamino)-1-(4-hydroxyphenyl)ethyl]cyclo-hexanol (I), and S(+)-1-[2-(Dimethylamino)-1-(4-hydroxyphenyl)ethyl]cyclohexanol or S(+)-4-[2-(Dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol, or one or more pharmaceutically acceptable salts or salt hydrates thereof, as well as pharmaceutical compns. utilizing these enantiomers and methods of using the enantiomers to treat, inhibit or control central nervous system disorders. To a soln. of 1-[2-(Dimethylamino)-1-(4-methoxyphenyl)ethyl]-cyclohexanol free base (prepn. given) in EtOAc at room temp. was added at once to a soln. of (+)-Di-para toluoyl-D-tartaric acid-monohydrate (DT(-)T) and was stirred at room temp. for 1 h. The resulting ppt. was filtered off, washed with EtOAc , dried overnight at 35? in a vacuum oven to provide crude R(-)-1-[2-(dimethylamino)-1-(4-methoxyphenyl)-ethyl]cyclohexanol DT(-)T salt (yield = 92.8%) as a white solid. The solid was recrystd., and treated with sodium hydroxide soln. to obtain I base which was sepd. and purified. Neurotransmitter uptake inhibition activity of the enantiomers were studied in rats. Pharmaceutical formulations of different enantiomers are disclosed.

IT **93413-62-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. and pharmaceutical formulation of enantiomers of desmethyl venlafaxine)

RN 93413-62-8 HCAPLUS

CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 27 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:111809 HCAPLUS
DOCUMENT NUMBER: 136:288525
TITLE: Distribution of venlafaxine and its O-desmethyl metabolite in human milk and their effects in breastfed infants
AUTHOR(S): Ilett, Kenneth F.; Kristensen, Judith H.; Hackett, L. Peter; Paech, Michael; Kohan, Rolland; Rampono, Jonathan
CORPORATE SOURCE: Department of Pharmacology, University of Western Australia, Nedlands, 6009, Australia
SOURCE: British Journal of Clinical Pharmacology (2002), 53(1), 17-22
CODEN: BCPHBM; ISSN: 0306-5251
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

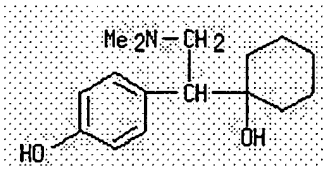
AB Aims: To characterize milk/plasma (M/P) ratio and infant dose, for venlafaxine (V) and its O-desmethyl metabolite (ODV), in breastfeeding

women taking venlafaxine for the treatment of depression, and to det. the plasma concn. and effects of these drugs in their infants. Methods: Six women (mean age 34.5 yr, mean wt. 84.3 kg) taking venlafaxine (median dose 244 mg day-1, range 225-300 mg day-1) and their seven infants (mean age 7.0 mo, mean wt. 7.3 kg) were studied. V and ODV in plasma and milk were measured by high-performance liq. chromatog. over a 12 h dose interval at steady-state. Infant exposure was estd. as the product of estd. milk prodn. rate (0.15 l kg-1 day-1) and av. drug concn. in milk, normalized to body wt. and expressed as a percentage of the wt.-adjusted maternal dose. Results: Mean M/PAUC values of 2.5 (range 2.0-3.2) and 2.7 (range 2.3-3.2) were calcd. for V and ODV, resp. The mean max. concns. (95% CI) of V and ODV in milk were 1161 (95% CI, 588, 1734) μg l-1 and 796 (362, 1230) μg l-1. Mean infant exposure was 3.2% (1.7, 4.7%) for V and 3.2% (1.9, 4.9%) for ODV (as V equiv.). V was detected in the plasma of one out of seven infants studied (5 μg l-1), while ODV was detected in four of the infants, at concns. ranging from 3 to 38 μg l-1. All of the infants in the study were healthy, as reported by their mothers and/or by clin. examn. on the study day. Conclusions: The concns. of V and ODV in breast milk were 2.5 and 2.7 times those in maternal plasma. The mean total drug exposure (as venlafaxine equiv.) of the breastfed infants was 6.4% (5.5-7.3%), which is below the 10% notional level of concern. There were no adverse effects in any of the infants. The data support the use of V in breastfeeding. Nevertheless, since low concns. of ODV were detected in the plasma of four out of the seven infants studied, we recommend breastfed infants should be monitored closely. Each decision to breast feed should be made as an individual risk:benefit anal.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(venlafaxine (Efexor) and metabolite O-desmethylvenlafaxine distribution in human milk and effect in breastfed infants)

RN 93413-62-8 HCAPLUS

CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



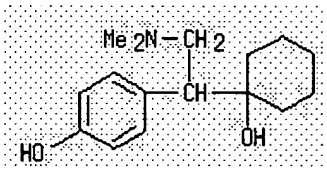
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:879760 HCAPLUS
DOCUMENT NUMBER: 136:145144
TITLE: Effect of antidepressants on ATP-dependent calcium uptake by neuronal endoplasmic reticulum
AUTHOR(S): Couture, L.; Elie, R.; Lavoie, P.-A.
CORPORATE SOURCE: Departement de pharmacologie, Universite de Montreal, Montreal, QC, H3C 3J7, Can.
SOURCE: Canadian Journal of Physiology and Pharmacology (2001), 79(11), 946-952
CODEN: CJPPA3; ISSN: 0008-4212
PUBLISHER: National Research Council of Canada

DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study investigated the effect of tricyclic and atypical antidepressants on ATP dependent calcium uptake by the endoplasmic reticulum of lysed synaptosomes from rat brain cortex. Tricyclic antidepressants (imipramine, desipramine, clomipramine, amitriptyline) exhibited no effect in the lower range (0.06 to 2 μM) of drug concns., and a concn.-dependent inhibition of calcium uptake in the upper range (6 to 200 μM). A concn.-dependent inhibition was obsd. for atypical antidepressants (mianserin, desmethylmianserin, venlafaxine, desmethylvenlafaxine, fluoxetine) in both the lower and the upper range of drug concns. Since no stimulation of calcium uptake was obsd. in either concn. range, it appears that the tricyclic and atypical antidepressants tested are not capable of normalizing, through their effect on the endoplasmic reticulum, an overactive calcium signal, which is possibly implicated in the etiol. of affective disorders. Also, although only marginal inhibition of calcium uptake is expected at brain concns. of tricyclics and mianserin-desmethylmianserin that are likely to be encountered during clin. use, a more substantial inhibition could occur with fluoxetine.
IT **93413-62-8**, O-Desmethylvenlafaxine
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effect of antidepressants on ATP-dependent calcium uptake by neuronal endoplasmic reticulum)
RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2000:900601 HCAPLUS
DOCUMENT NUMBER: 134:56475
TITLE: Preparation and formulation of O-desmethyl venlafaxine enantiomers
INVENTOR(S): Yardley, John Patrick; Asselin, Andre Alfred
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076955	A1	20001221	WO 2000-US16388	20000614

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,

ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,
SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

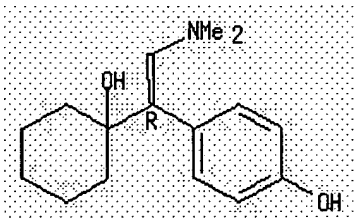
PRIORITY APPLN. INFO.: US 1999-183029P P 19990615
US 1999-333594 A 19990615

AB Title compds. were prepd. by optical resoln. of venlafaxine followed by O-demethylation. Data for biol. activity of title compds. were given.

IT **142761-11-3P** **142761-12-4P** **313471-76-0P**,
(R)-(-)-O-Desmethylvenlafaxine fumarate hydrate **313474-92-9P**,
(S)-(+)-O-Desmethylvenlafaxine fumarate hydrate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and formulation of O-desmethyl venlafaxine enantiomers)

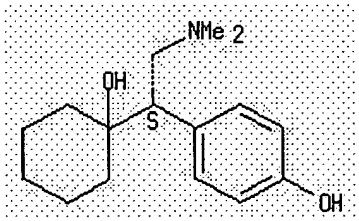
RN 142761-11-3 HCAPLUS
CN Phenol, 4-[(1R)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 142761-12-4 HCAPLUS
CN Phenol, 4-[(1S)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

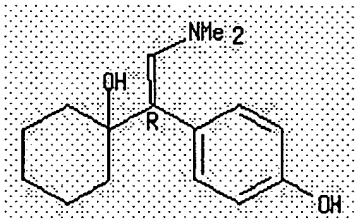


RN 313471-76-0 HCAPLUS
CN Phenol, 4-[(1R)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]-, (2E)-2-butenedioate (1:1) (salt), monohydrate (9CI) (CA INDEX NAME)

CM 1

CRN 142761-11-3
CMF C16 H25 N O2

Absolute stereochemistry. Rotation (-).



CM 2

CRN 110-17-8
CMF C4 H4 O4

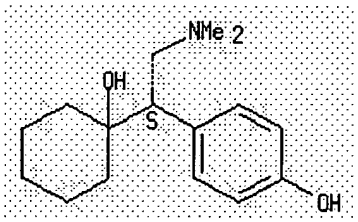
Double bond geometry as shown.

RN 313474-92-9 HCAPLUS
CN Phenol, 4-[(1S)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]-, (2E)-2-butenedioate (1:1) (salt), monohydrate (9CI) (CA INDEX NAME)

CM 1

CRN 142761-12-4
CMF C16 H25 N O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:725583 HCAPLUS
DOCUMENT NUMBER: 133:296268
TITLE: Preparation of derivatives of venlafaxine and their inhibition of neuronal monoamine reuptake
INVENTOR(S): Jerussi, Thomas P.; Senanayake, Chrisantha H.
PATENT ASSIGNEE(S): Sepracor Inc., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2

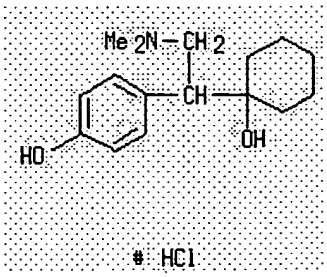
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059851	A1	20001012	WO 2000-US8705	20000331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2368083	AA	20001012	CA 2000-2368083	20000331
EP 1165487	A1	20020102	EP 2000-920026	20000331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003521470	T2	20030715	JP 2000-609367	20000331
NZ 514612	A	20040130	NZ 2000-514612	20000331
EP 1466889	A1	20041013	EP 2004-10248	20000331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
AU 782092	B2	20050630	AU 2000-40627	20000331
NO 2001004816	A	20011204	NO 2001-4816	20011003
US 2004106576	A1	20040603	US 2003-720134	20031125
US 2005197392	A1	20050908	US 2005-91518	20050329

PRIORITY APPLN. INFO.:		
US 1999-127938P	P	19990406
US 1999-167906P	P	19991130
US 2000-527442	A3	20000317
EP 2000-920026	A3	20000331
WO 2000-US8705	W	20000331
US 2003-720134	A3	20031125

AB Prepn. of derivs. of venlafaxine, e.g., O-desmethylvenlaflaxine, is described. Also disclosed are methods of treating and preventing diseases and disorders including, but not limited to, affective disorders such as depression, bipolar and manic disorders, attention deficit disorder, attention deficit disorder with hyperactivity, Parkinson's disease, epilepsy, cerebral function disorders, obesity and wt. gain, incontinence, dementia and related disorders.

IT **300827-87-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of derivs. of venlafaxine and their inhibition of neuronal monoamine reuptake)
RN 300827-87-6 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

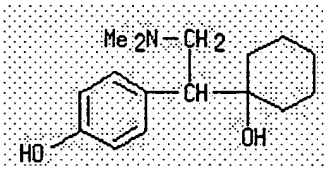
L4 ANSWER 31 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:700645 HCAPLUS
DOCUMENT NUMBER: 134:163
TITLE: CYP2B6 mediates the in vitro hydroxylation of bupropion: potential drug interactions with other antidepressants
AUTHOR(S): Hesse, Leah M.; Venkatakrishnan, Karthik; Court, Michael H.; Von Moltke, Lisa L.; Duan, Su X.; Shader, Richard I.; Greenblatt, David J.
CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, New England Medical Center, Tufts University School of Medicine, Boston, MA, 02111, USA
SOURCE: Drug Metabolism and Disposition (2000), 28(10), 1176-1183
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The in vitro biotransformation of bupropion to hydroxybupropion was studied in human liver microsomes and microsomes contg. heterologously expressed human cytochromes P 450 (CYP). The mean (?S.E.) Km in four human liver microsomes was 89 (?14) μM. In microsomes contg. cDNA-expressed CYPs, hydroxybupropion formation was mediated only by CYP2B6 at 50 μM bupropion (Km 85 μM). A CYP2B6 inhibitory antibody produced more than 95% inhibition of bupropion hydroxylation in four human livers. Bupropion hydroxylation activity at 250 μM was highly correlated with S-mephenytoin N-demethylation activity (yielding nirvanol), another CYP2B6-mediated reaction, in a panel of 32 human livers (r = 0.94). The CYP2B6 content of 12 human livers highly correlated with bupropion hydroxylation activity (r = 0.96). Thus bupropion hydroxylation is mediated almost exclusively by CYP2B6 and can serve as an index reaction reflecting activity of this isoform. IC50 values for inhibition of a CYP2D6 index reaction (dextromethorphan O-demethylation) by bupropion and hydroxybupropion were 58 and 74 μM, resp. This suggests a low inhibitory potency vs. CYP2D6, the clin. importance of which is not established. Since bupropion is frequently coadministered with other antidepressants, IC50 values (μM) for inhibition of bupropion hydroxylation were detd. as follows: paroxetine (1.6), fluvoxamine (6.1), sertraline (3.2), desmethylsertraline (19.9), fluoxetine (59.5), norfluoxetine (4.2), and nefazodone (25.4). Bupropion hydroxylation was only weakly inhibited by venlafaxine, O-desmethylvenlafaxine, citalopram, and desmethylcitalopram. The inhibition of bupropion hydroxylation in vitro by a no. of newer antidepressants suggests the potential for clin. drug interactions.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(CYP2B6 mediates in vitro hydroxylation of bupropion: potential drug interactions with other antidepressants)
RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 32 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2000:384124 HCAPLUS
DOCUMENT NUMBER: 133:17270
TITLE: Preparation of (-)-venlafaxine and derivatives as neuronal monoamine reuptake inhibitors.
INVENTOR(S): Jerussi, Thomas P.; Senanayake, Chrisantha H.
PATENT ASSIGNEE(S): Sepracor Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032556	A1	20000608	WO 1999-US28303	19991201
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6342533	B1	20020129	US 1999-450690	19991130
CA 2352324	AA	20000608	CA 1999-2352324	19991201
EP 1135359	A1	20010926	EP 1999-968056	19991201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003524613	T2	20030819	JP 2000-585198	19991201
AU 774408	B2	20040624	AU 2000-24749	19991201
US 2002086904	A1	20020704	US 2001-14592	20011214
US 6441048	B2	20020827		
US 2003018083	A1	20030123	US 2002-222815	20020819
US 6911479	B2	20050628		
US 2004180952	A1	20040916	US 2004-806423	20040323
PRIORITY APPLN. INFO.:			US 1998-110488P	P 19981201

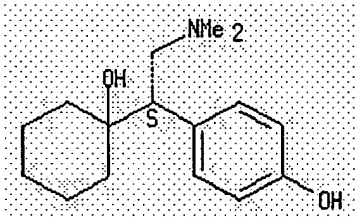
US 1999-450690	A	19991130
WO 1999-US28303	W	19991201
US 2001-14592	A3	20011214
US 2002-222815	A3	20020819

AB A pharmaceutical compn. comprising (-)-venlafaxine deriv. substantially free of (+)-stereoisomer is claimed. Thus, (?)-venlafaxine in THF was added to a mixt. prepd. from Ph2PH and BuLi in THF at 0? followed by stirring and overnight reflux to give 73.8% (?)-O-desmethylvenlafaxine, which was resolved using di-p-toluoyl-L-tartaric acid to give (-)-O-desmethylvenlafaxine. Drug formulations contg. the latter are given.

IT **142761-12-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (-)-venlafaxine and derivs. as neuronal monoamine reuptake inhibitors)

RN 142761-12-4 HCAPLUS
CN Phenol, 4-[(1S)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 33 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:384122 HCAPLUS
DOCUMENT NUMBER: 133:30575
TITLE: Preparation of derivatives of (+)-venlafaxine as inhibitors of neuronal monoamine reuptake.
INVENTOR(S): Jerussi, Thomas P.; Senannayake, Chrisantha H.
PATENT ASSIGNEE(S): Sepracor Inc., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032555	A1	20000608	WO 1999-US28306	19991201

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,

DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

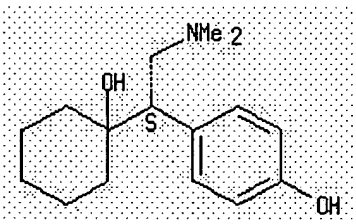
US 6197828	B1	20010306	US 1999-450691		19991130
CA 2352321	AA	20000608	CA 1999-2352321		19991201
EP 1135358	A1	20010926	EP 1999-965065		19991201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2003501344	T2	20030114	JP 2000-585197		19991201
PRIORITY APPLN. INFO.:			US 1998-110486P	P	19981201
			US 1999-450691	A	19991130
			WO 1999-US28306	W	19991201

AB A method of treating an affective disorder comprises administration of a (+)-venlafaxine deriv. substantially free of the (-)-enantiomer. Thus, (?)-venlafaxine (prepn. given) was added to a 0? mixt. of Ph2PH and BuLi followed by stirring and reflux overnight to give 73.8% (?)-O-desmethylvenlafaxine, which was resolved to give (+)-O-desmethylvenlafaxine. Drug formulations contg. the latter are given.

IT **142761-12-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of derivs. of (+)-venlafaxine as inhibitors of neuronal monoamine reuptake)

RN 142761-12-4 HCAPLUS
CN Phenol, 4-[(1S)-2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 34 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:534794 HCAPLUS
DOCUMENT NUMBER: 129:156948
TITLE: Modifying the behavior of dogs exhibiting canine affective aggression with R and S enantiomers or racemic mixtures of selective serotonin reuptake inhibitors or their metabolites
INVENTOR(S): Dodman, Nicholas H.
PATENT ASSIGNEE(S): Trustees of Tufts College, USA
SOURCE: U.S., 21 pp., Cont.-in-part of U.S. 5,554,383.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 5788986	A	19980804	US 1996-699112	19960816
US 5554383	A	19960910	US 1995-417747	19950406
PRIORITY APPLN. INFO.:			US 1995-417747	A2 19950406

AB A veterinary method for clin. modifying the behavior of a household pet dog exhibiting a recognized type of canine affective aggression behavior is provided. The veterinary behavior modification method administers at least one compd. selected from the group consisting of R enantiomers, S enantiomers, or a racemic mixt. of selective serotonin reuptake inhibitors or their active metabolites to the dog upon one or multiple occasions; and the administration of these compds. will modify clin. the canine affective aggression behavior of the household dog permanently or for an indefinite period of time. This veterinary behavior modification method can be usefully employed as an adjunct to conditioning approaches presently employed and will avoid the need for euthanasia in extreme behavioral circumstances.

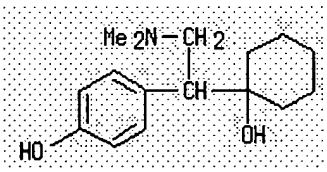
IT **93413-62-8**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(modifying the behavior of aggressive dogs with R and S enantiomers or racemic mixts. of selective serotonin reuptake inhibitors or their metabolites)

RN 93413-62-8 HCAPLUS

CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER:	1997:681434 HCAPLUS
DOCUMENT NUMBER:	127:355027
TITLE:	Application of a first-pass effect model to characterize the pharmacokinetic disposition of venlafaxine after oral administration to human subjects
AUTHOR(S):	Taft, David R.; Iyer, Ganesh R.; Behar, Leon; DiGregorio, Robert V.
CORPORATE SOURCE:	Division of Pharmaceutics and Industrial Pharmacy, Long Island University, Brooklyn, NY, 11201, USA
SOURCE:	Drug Metabolism and Disposition (1997), 25(10), 1215-1218 CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER:	Williams & Wilkins
DOCUMENT TYPE:	Journal
LANGUAGE:	English

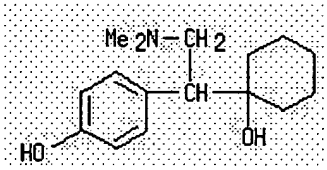
AB Venlafaxine (VEN), a drug used in the treatment of depression, undergoes significant first-pass metab. after oral dosing to O-desmethylvenlafaxine (ODV), a metabolite with comparable therapeutic activity to that of parent drug. The pharmacokinetic disposition of VEN was characterized using a "first-pass" model that incorporates a presystemic compartment (liver) to

account for the first-pass metab. of VEN to ODV. A series of differential equations were simultaneously fitted to plasma concns. of parent and metabolite. A good fit of the model to obsd. data was demonstrated, generating ests. for the following parameters: ka (1.31 h-1), VVEN (252 L), CLint (65.8 L/h), RL (liver:plasma partition coeff., 29.6), VODV (181 L), and CLODV (23.5 L/h). Parameter ests. correlated closely with those obtained through noncompartmental methods. These results indicate that the time-course disposition of a compd. undergoing first-pass hepatic metab. after oral dosing can be successfully modeled.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); **THU (Therapeutic use)**; BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); USES (Uses)
(application of a first-pass effect model to characterize the pharmacokinetic disposition of venlafaxine after oral administration to human subjects)

RN 93413-62-8 HCAPLUS

CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 36 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

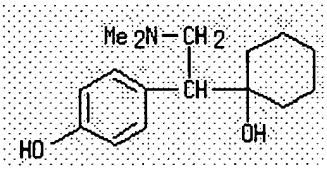
Full Text | Citing References

ACCESSION NUMBER: 1997:43252 HCAPLUS
DOCUMENT NUMBER: 126:139312
TITLE: Central & peripheral nervous systems. Venlafaxine: a novel antidepressant compound
AUTHOR(S): Schweizer, Edward; Thielen, Richard J.; Frazer, Alan
CORPORATE SOURCE: Dep. Psychiary, Univ. Pennsylvania Sch. Med., Philadelphia, PA, 19104, USA
SOURCE: Expert Opinion on Investigational Drugs (1997), 6(1), 65-78
CODEN: EOIDER; ISSN: 0967-8298
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 89 refs. Venlafaxine is a new antidepressant that inhibits the reuptake of both 5-hydroxytryptamine (serotonin; 5-HT) and noradrenaline (NA). It is somewhat more potent as an inhibitor of the reuptake of 5-HT than NA. Its potency to inhibit the reuptake of 5-HT is comparable to that of tricyclic antidepressants (TCAs) such as amitriptyline or imipramine, but it is less potent than these drugs at inhibiting the reuptake of NA. Consequently, at low doses, venlafaxine may be a more effective inhibitor of the reuptake of 5-HT than that of NA. The major metabolite of venlafaxine in humans, O-desmethylvenlafaxine, has comparable potency to the parent drug for inhibiting the reuptake of either NA or 5-HT in vitro, but it is less potent in vivo. Both venlafaxine and O-desmethylvenlafaxine are essentially devoid of activity at muscarinic cholinergic, H1 histaminergic, and β1-adrenoceptors. This probably account for venlafaxine having a side-effect profile similar

to that of selective serotonin reuptake inhibitors (SSRIs) rather than that of TCAs. Venlafaxine is subject to extensive first-pass metab. and is metabolized by the cytochrome P 450 isoenzyme IID6 in the liver. The half-life of venlafaxine is 3-4 h and that of its principal metabolite is about 10 h. The daily dose of venlafaxine can be administered as either two or three divided doses without altering significantly the pharmacokinetics of venlafaxine. The most common side-effects of venlafaxine are nausea, sedation, and dizziness, dry mouth and sweating, as well as sexual dysfunctions, primarily problems with erection and delayed ejaculation. In some patients, venlafaxine also caused sustained elevations in both systolic and diastolic blood pressure; this effect is dose-dependent. Venlafaxine is much safer in over-dosage than the TCAs. Antidepressant efficacy of venlafaxine has been found in out-patients and in-patients. In general, its efficacy is comparable to that of comparator drugs (primarily TCAs or SSRIs), and in some cases even greater, and its efficacy is greater than that measured with placebo.

IT **93413-62-8**, O-Desmethylvenlafaxine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); **THU (Therapeutic use)**; BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(venlafaxine antidepressant activity and pharmacokinetics in humans)
RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

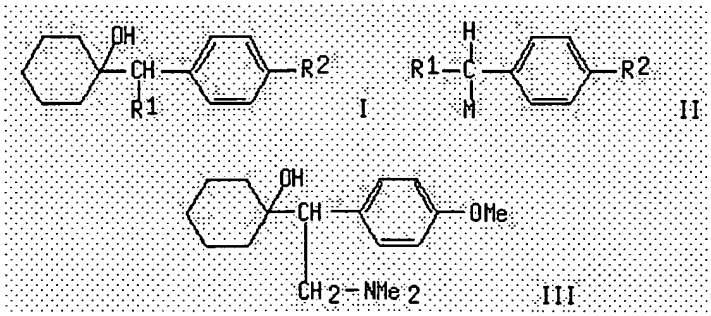
L4 ANSWER 37 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1991:81228 HCAPLUS
DOCUMENT NUMBER: 114:81228
TITLE: Preparation of cyclohexanol derivatives as intermediates for antidepressants
INVENTOR(S): Shepherd, Robin Gerald
PATENT ASSIGNEE(S): John Wyeth and Brother Ltd., UK
SOURCE: Brit. UK Pat. Appl., 15 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
GB 2227743	A1	19900808	GB 1990-2095		19900130
GB 2227743	B2	19920617			
US 5043466	A	19910827	US 1990-471187		19900126
PRIORITY APPLN. INFO.:			GB 1989-2209	A	19890201

OTHER SOURCE(S): CASREACT 114:81228; MARPAT 114:81228
GI

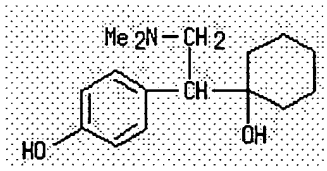


AB Title compds. I [R1 = cyano, CONMe2, CSNMe2; R2 = OMe, (protected) OH], useful as intermediates for prepn. of antidepressants, were prepd. by reaction of II [M = Li, Na, K, or MgX (X = halo); R2 = OMe, protected OH] with cyclohexanone in hydrocarbon/ether solvents. For example, II (R1 = CSNMe2, R2 = OMe, M = MgBr) gave the corresponding I in 64% yield. Subsequent redn. of I by Raney-Ni gave the antidepressant (no data) N,N-dimethyl-2-(1-hydroxycyclohexyl)-2-(4-methoxyphenyl)ethylamine (III).

IT **93413-62-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antidepressant)

RN 93413-62-8 HCAPLUS

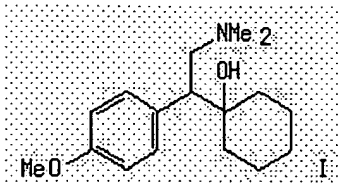
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 38 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

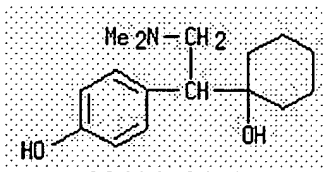
ACCESSION NUMBER: 1990:630878 HCAPLUS
DOCUMENT NUMBER: 113:230878
TITLE: 2-Phenyl-2-(1-hydroxycycloalkyl)ethylamine derivatives: synthesis and antidepressant activity
AUTHOR(S): Yardley, John P.; Husbands, G. E. Morris; Stack, Gary; Butch, Jacqueline; Bicksler, James; Moyer, John A.; Muth, Eric A.; Andree, Terrance; Fletcher, Horace, III; et al.
CORPORATE SOURCE: Wyeth-Ayerst Res., Princeton, NJ, 08543-8000, USA
SOURCE: Journal of Medicinal Chemistry (1990), 33(10), 2899-905
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:230878
GI



AB A series of 2-phenyl-1-(1-hydroxycycloalkyl)ethylamine derivs. was examd. for the ability to inhibit both rat brain imipramine receptor binding and the synaptosomal uptake of norepinephrine (NE) and serotonin (5-HT). Neurotransmitter uptake inhibition was highest for a subset of 2-phenyl-2-(1-hydroxycyclohexyl)dimethylethylamines in which the aryl ring has a halogen or methoxy substituent at the 3- and/or 4-positions. Potential antidepressant activity in this subset was assayed in three rodent models-the antagonism of reserpine-induced hypothermia, the antagonism of histamine-induced ACTH release, and the ability to reduce noradrenergic responsiveness in the rat pineal gland. An acute effect seen in the rat pineal gland with several analogs, including 1-[1-(3,4-dichlorophenyl)-2-(dimethylamino)ethyl]cyclohexanol and 1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol (I), was taken as a possible correlate of a rapid onset of antidepressant activity. Compd. I (venlafaxine) is presently undergoing clin. evaluation.

IT **93413-62-8P** **93414-04-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and antidepressant activity of)

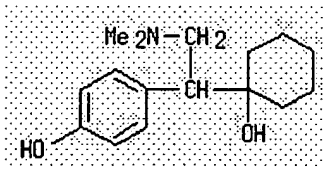
RN 93413-62-8 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA INDEX NAME)



RN 93414-04-1 HCAPLUS
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 93413-62-8
CMF C16 H25 N O2



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.


E
HO2C
CO2H

=>